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THE TECHNIQUE OF MITRAL VALVULOTOMY

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HALF a century has elapsed since Samways,[12] and later Brunton,[4] suggested that mitral stenosis could be attacked surgically. The earliest clinical attempts to excise a portion of the rigid valvular orifice were made by Cutler in 1923,[7] and in the ensuing few years he and others made further attempts to develop the procedure of mitral valvulotomy.

In 1929 there were ten collected cases with an operative mortality of 80 per cent,[8] but Cutler stated, "It is our conclusion that the mortality figures alone should not deter further investigation, both clinical and experimental, since they are to be expected in the opening up of any new field of surgical endeavor."

Of particular interest was the patient in whom Souttar[15] digitally dilated the stenotic valve through the auricular appendage and the patient was well six years later. This single successful case did not alter the dismal picture presented by the group, thus discouraging further clinical attempts for the next two decades.

As a consequence of a number of recent developments in the field of cardiovascular surgery, interest has been revived in the surgical treatment of mitral stenosis. Two general lines of approach have been developed, one indirect and the other direct. The former includes methods designed to alleviate the symptoms of pulmonary hypertension by various intra- and extracardiac shunts,[3, 9] by surgically produced tricuspid insufficiency,[6] or by vena caval ligation.[6] Although the indirect techniques have afforded temporary relief in some instances, they have been generally unsatisfactory. The direct approach to the problem by valvulotomy, on the other hand, has produced encouraging and often striking results. Credit for the recent advances belongs to Smithy,[14] Bailey,[1] Harken,[9] and Brock.[2]

Much of the success in mitral valvulotomy is attributable to the more accurate understanding of the function and mechanism of the mitral valve during the cardiac cycle. It is now clear that the anteromedial and posterolateral leaflets themselves should not be altered during an operative procedure if a

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crippling mitral insufficiency is to be avoided. The anteromedial leaflet is of particular importance in this regard, for it serves the vital function of baffling the blood into the ventriculo-aortic outflow tract and prevents reflux into the atrium. All workers are now agreed that an increase in area of valve orifice must be obtained at the commissures where the leaflets are fused to one another. Thus, the essential objective of valvulotomy consists in separation of the fused valve leaflets at the commissures, particularly anterolaterally, in order to secure maximum increase in the valve opening, while at the same time restoring valvular action with minimal regurgitation. Various technical methods have been proposed for achieving this objective, and the operation is still undergoing evolutionary developments. With accumulated experience and the spread of interest in the problem, improvements and modifications in technique will gradually lead to the development of the most effective surgical procedure. Accordingly, this report is concerned with the technique which has been employed by us in a series of twenty-one consecutive cases of mitral stenosis with one fatality.

PREPARATION FOR SURGERY

Most patients submitted for surgery have been on a prolonged regimen of digitalis and salt deprivation, and this program is maintained. Mecurial diuretics may be administered two to three times weekly if necessary, and usually on the day preceding operation. There is convincing experimental[10] and clinical[5] evidence to support the use of quinidine in patients with heart disease undergoing anesthesia, and particularly in the presence of severe cardiac damage, to diminish cardiac irritability and eliminate certain prefibrillation states during anesthesia. On the date prior to operation, a test dose of quinidine sulfate, 0.03 Gm., is administered orally. If there is no reaction to the test dose, an oral dose of quinidine sulfate, 0.80 Gm., is given on the morning of operation about two hours before surgery. All patients receive procaine penicillin injections twenty-four hours, and again several hours, before operation. Preanesthetic medications are otherwise similar to those used for any major operation.

ANESTHETIC CONSIDERATIONS

Anesthesia is induced with nitrous oxide, or, in some instances, with Pentothal Sodium, a 2½ per cent solution given intravenously. Surgical levels of anesthesia are maintained with a mixture of ether in high concentrations of oxygen in a closed to-and-fro system. Constant attention is required of the anesthetist in order to maintain maximum pulmonary ventilation and a steady level of anesthesia, and also to give prompt assistance if cardiac failure ensues. Special medications under anesthesia are avoided. Intravenous procaine or procaine amide are not used in the usual case, but may be employed if disturbing arrhythmias result. Some authors advocate liberal use of procaine hydrochloride solutions for intravenous infusions, pericardial instillations, and myocardial infiltrations to reduce cardiac irritability. From our own experience, it appears that procaine by any of these routes is unnecessary and that small preoperative

doses of quinidine sulfate are effective in preventing arrhythmias during operation. Quinidine lactate is always available for intravenous use in case of paroxysmal ventricular tachycardia, disturbing ventricular extrasystoles, or ventricular fibrillation. Supplemental atropine administered during anesthesia is inadvisable, because an induced tachycardia in patients with mitral stenosis may lead to pulmonary edema. Excessive bronchial secretions may be troublesome but should be removed by frequent tracheal aspirations.

Fig. 1.—Photograph showing patient and healed incision ten days after operation.

OPERATIVE PROCEDURE

The anesthetized patient lies supine on the operating table and, after tracheal intubation, the left shoulder is elevated on a folded towel. The left arm is suspended from an overhead support by means of adhesive strips applied to the hand and forearm. This position provides maximum exposure of the anterolateral aspect of the left chest. A curved submammary incision is made, and the thorax is entered through the fourth intercostal space (Figs. 1 and 2). The fourth costal cartilage is divided lateral to the internal mammary vessels. Occasionally one encounters an extensive obliteration of the pleural space as a result, usually, of recurrent pleuropulmonary inflammation. By a careful dissection sufficient area of lung is mobilized to expose the mediastinum and pericardium. When a self-retaining rib retractor is opened, adequate exposure is provided.

Traction sutures of fine silk are placed in the pericardium immediately over the sulcus between the auricular appendage and the distended common pulmonary artery, and the pericardium is opened between them (Fig. 2,*a*). There is usually a small amount of pericardial fluid which escapes. The pericardial incision is extended caudally, parallel, and usually anterior, to the phrenic

nerve to a point a few centimeters below the atrioventricular junction (Fig. 2,*a*). In order to provide better exposure of the atrium, T-shaped extensions of the incision in the pericardium are made at each end. The resulting anterior and posterior pericardial flaps are retracted by means of temporary traction sutures (Fig. 2,*b*). This type of opening in the pericardium permits maximum exposure of the auricle without risk of herniation of the ventricle.

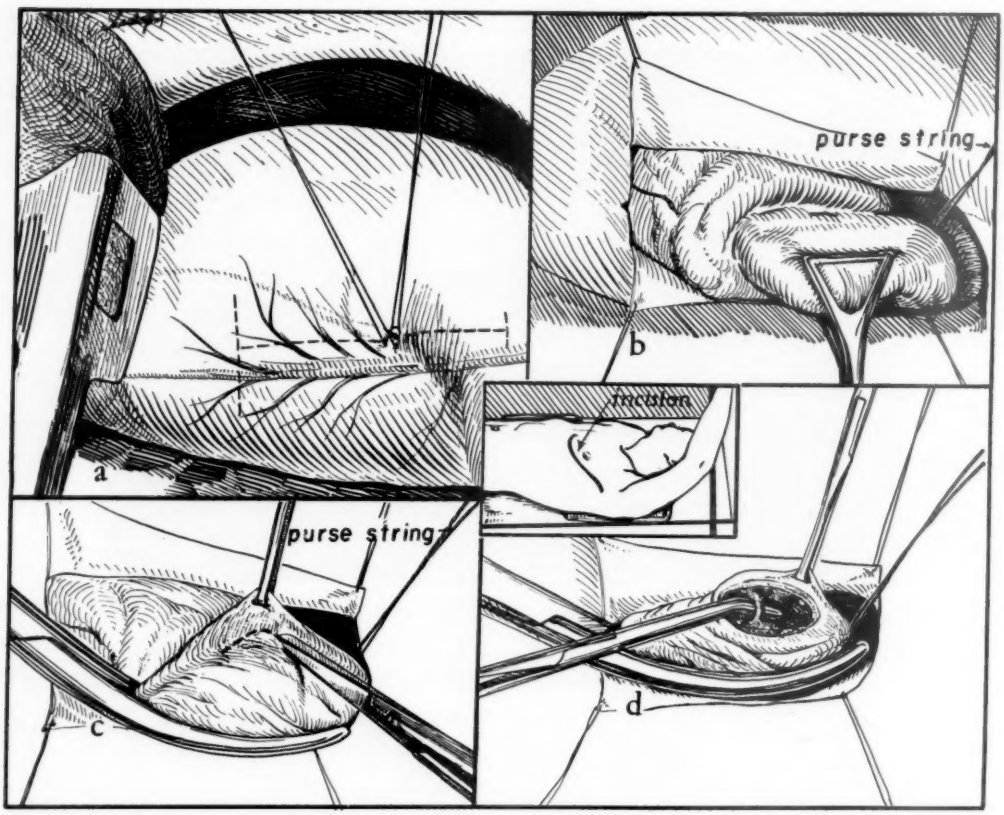

Fig. 2, *a-d*.—Drawing showing steps in operation for mitral valvulotomy. Insert shows patient lying in supine position with the left shoulder slightly elevated on a folded towel and left arm suspended from an overhead support.

a, Traction sutures of fine silk are placed in the pericardium to facilitate the pericardial entry immediately over the sulcus between the auricular appendage and the distended pulmonary artery. The incision in the pericardium is represented by the dotted lines with T-shaped extensions at each end to provide additional exposure of the heart. *b*, Traction sutures are placed in the anterior and posterior pericardial flaps to permit their retraction and maximum exposure of the auricle. An atraumatic Pennington type clamp is applied to the tip of the auricular appendage and a purse-string suture of 0 black silk is placed around the base of the auricle. *c*, A nontraumatic clamp with long, slightly curved jaws is applied across the base of the appendage to occlude its lumen, and an incision of sufficient length only to accommodate the index finger is made on the lateral surface of the appendage near its apex. *d*, Intraluminal trabeculations are carefully divided to permit ready entry of the finger.

Direct pressure recordings are made from the left auricle, pulmonary artery, and aorta by inserting a 20 gauge needle attached to a length of flexible ureteral catheter which is connected with a Sanborn electromanometer. Pressure tracings are made with simultaneous electrocardiograms. Bleeding from the needle hole in these vessels is controlled by light pressure. At the completion of the pressure determinations, the chest retractor is temporarily re-

leased and the lungs are inflated. After reinsertion of the rib spreader, the tip of the auricular appendage is steadied with an atraumatic forceps and a purse-string suture of 0 black silk is placed about the auricular base. Care must be used not to pierce the endocardium (Fig. 2,*b*). The ends of the purse-string suture are marked with a small clamp and laid aside. A special nontraumatic clamp is applied across the base of the appendage, and the handle is closed to the first notch on the ratchet. An incision is made on the lateral surface of the appendage near its apex (Fig. 2,*c*). It is important to make this incision sufficiently long to accommodate the index finger snugly. Intraluminal trabeculations are divided to complete the incision and to allow unobstructed entry into the auricle (Fig. 2,*d*).

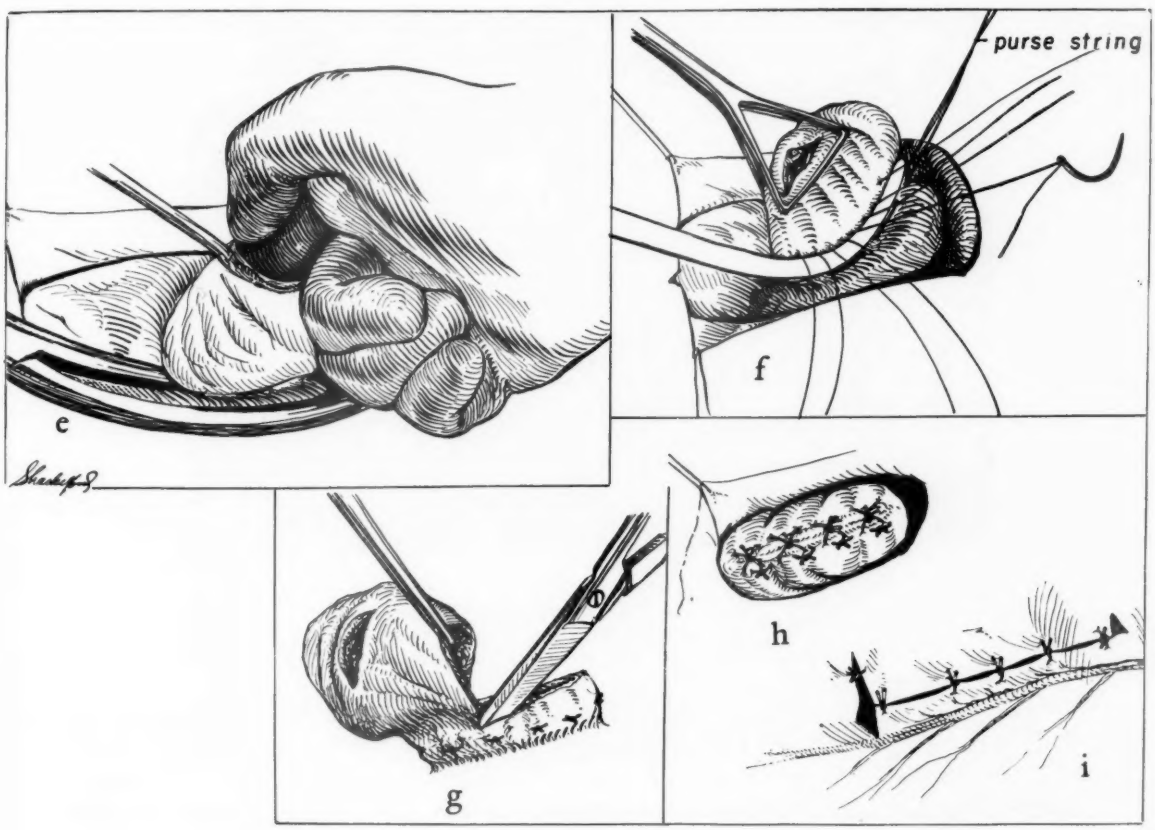

Fig. 2, *e-i*.—*e*, The right index finger is inserted into the opening made in the auricular appendage as the occlusive clamp is released by the left hand. *f*, Following intracardiac manipulation the occlusive clamp is reapplied to the auricle as the right index finger is withdrawn. A row of mattress sutures of fine silk is applied to the base of the auricular appendage close to the occlusive clamp. *g*, The purse-string suture is removed and the mattress sutures are tied. The auricular appendage is amputated distal to the row of sutures. *h*, A second row of interrupted figure-of-eight sutures is used to approximate the cut edges of the auricle. *i*, The pericardial incision is closed loosely with interrupted sutures of fine silk.

The possible presence of a mural thrombus should be considered and, if encountered, it may be dislodged and withdrawn as the auricular clamp is carefully released. In such cases it is always advisable to open the auricular clamp

momentarily to allow a forceful gush of blood to eject any other loose thrombi. As an additional precaution in cases in which thrombi are encountered, the anesthetist compresses the carotid vessels to minimize the danger of cerebral embolism during the ensuing intra-auricular manipulations.

With his left hand, the operator releases the auricular clamp as he inserts his right index finger into the auricular incision (Fig. 2,*e*). Blood loss at this stage and subsequently is minimal, and traction on the purse-string suture is not necessary if the auricular incision has been made so that it fits the finger closely. In no instance has the purse-string suture been necessary to control hemorrhage during the actual valvulotomy. With experience one can quickly find the mitral orifice and determine its relative size, degree of mitral regurgitation, the presence or absence of calcification, and the elasticity of the valve leaflets (Fig. 3). In favorable cases, the anteromedial leaflet is supple and

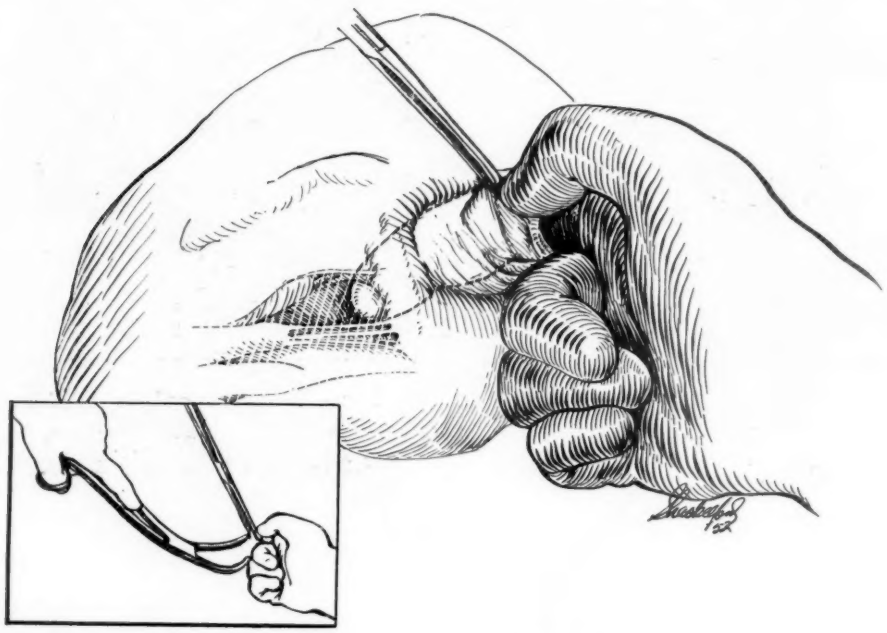

Fig. 3.—Drawing showing intracardiac position of index finger during exploration and division of the commissures. Insert shows the technique of insertion and withdrawal of the finger into the appendage and the method of handling the atraumatic auricular clamp.

bulges into the atrium during ventricular systole. After preliminary exploration of the mitral orifice, the finger is introduced through the fibrous opening. In most instances the finger may be passed almost to the level of the proximal interphalangeal joint. The finger is withdrawn into the atrium temporarily to permit ventricular filling and then reinserted and the commissure is digitally dissected or torn in the line of fusion. Customarily, the longer anterolateral commissure splits better than the shorter posteromedial one, but both commissures should be divided where possible. The amount of regurgitation through the new orifice is determined before the finger is withdrawn.

In the majority of instances, a satisfactory valvulotomy does not require the aid of the valvulotome, but in approximately 10 to 15 per cent of the cases

a cutting instrument may be useful. In such cases there may be calcification, or the fibrosis may tend to be more extensive with involvement of the entire valve leaflets and the chordae tendineae, giving the examiner the impression of a dense fibrous cone. Under such circumstances, an actual incision at the commissure may offer the only possibility of separating the leaflets. The Sellors fingernail knife[13] is a practical instrument for these cases and, because the sensitive volar surface of the finger is not widely covered by a metal surface as in other types of valvulotomes, offers the advantage of combining digital mobility and accurate control of the blade (Fig. 4). The initial incision may be extended in the line of the commissures by a combination of sharp and blunt dissection, retracting the blade of the instrument as necessary. In any event, the mitral orifice should never be occluded for more than three or four heartbeats.

Fig. 4.—Photograph showing the Sellors fingernail knife which is useful in incising the commissures in difficult cases. The curved blade may be advanced or withdrawn within a protective sheath by means of a plunger and cable from an ordinary small photographic camera. The fingernail knife is held in place on the finger by a second glove which is applied over the instrument and perforated at the finger tip to expose the blade.

As the finger is withdrawn, the operator closes the auricular clamp across the base of the orifice permitting minimal blood loss (Fig. 3). With this method of introduction and withdrawal of the finger, a number of explorations may be made by the surgeon or his assistant with relative safety. Following completion of the valvulotomy, a high amputation of the auricular appendage is done to eliminate the pouch in the atrial wall which may predispose to thrombosis. Mass ligature of the appendage is undesirable, and the atrial defect is preferably closed by a row of interrupted mattress sutures and additional figure-of-eight sutures over the cut edges of the muscle producing a neat suture line on the endocardial surface (Fig. 2,*f*, *g*, and *h*). The excised auricular appendage is preserved for histologic examination to determine the presence or absence of the features of rheumatic myocarditis. In a few such specimens, a chronic inflammatory process with some round-cell infiltration, particularly in the subendocardial space, has been demonstrated.

Pressure recordings from the left auricle, pulmonary artery, and aorta are repeated. In most cases, the pressures recorded in the left auricle have shown a significant drop, and the tracing indicates little if any mitral insufficiency. Pulmonary arterial pressure is diminished, and aortic pressure is either unchanged or slightly increased.

The pericardial incision is closed with multiple interrupted fine silk sutures, allowing at least one opening through which pericardial accumulations of fluid may drain into the pleural space to prevent a possible cardiac tamponade (Fig. 2,*i*). A lung biopsy is taken from the lingula for histologic study to determine the presence and degree of pulmonary changes considered to be characteristic of mitral stenosis.[11]

The chest is closed in layers of interrupted unabsorbable sutures, and an intercostal tube is inserted for water-sealed drainage. During the operative procedure, most patients have received approximately 500 c.c. of blood. The patient's condition at the completion of operation is often strikingly improved.

POSTOPERATIVE MANAGEMENT

In the majority of instances, these patients present no special postoperative problems. Mild shock has occurred in some patients, and particularly in the older patients with advanced cardiac disturbances. In the majority of these, an infusion of 5 per cent dextrose in distilled water is all that is required, but whenever necessary a gradual transfusion has been administered. Pulmonary edema has occurred in less than one-half of the cases and has usually been mild. In most instances, patients are already fully digitalized, but it may be necessary to increase the digitalis and to administer mercurial diuretics. Salt deprivation is continued postoperatively. In one patient who developed a severe inflammatory pericarditis, auricular fibrillation, and pulmonary edema, venous tourniquets were rotated on the extremities and proved to be beneficial. Auricular fibrillation developed in four patients after operation. In all but one, the fibrillation was converted to a sinus rhythm by the administration of quinidine sulfate for twenty-four to forty-eight hours in therapeutic doses ranging up to 1.0 Gm. every four hours. In the remaining case quinidine was not employed because the patient found it inconvenient to come into the hospital for this purpose. Recently, it has become our policy to give quinidine to all patients who had a sinus rhythm before operation, as prophylaxis against the development of auricular fibrillation after operation. The prophylactic dosage we employ is 0.2 Gm. every four hours.

In the majority of instances, it is possible to detect a pericardial friction rub for two to three days after operation, but in only two patients has the rub persisted for more than one week. In one of the early cases in which 4 per cent procaine hydrochloride was instilled into the pericardium, a severe inflammatory pericarditis was produced, presumably because the procaine hydrochloride was not buffered (pH 4.3). Because of this experience and because of the evidence that procaine topically is ineffectual, the use of procaine in the pericardium has been discontinued. A mild atelectasis occurred in two cases, but responded to

conservative measures without bronchoscopy. There is a greater tendency for atelectasis to occur in the left lung, particularly in those cases where the left atrium is overdistended and encroaches upon the left main bronchus. Embolism after operation may be a serious threat to patients and, therefore, in every case a careful examination is made immediately after the operation to determine the presence of all peripheral pulses. In two of our cases embolism has occurred after operation. In one patient a pulmonary infarction in the left upper lobe was discovered several hours after operation. The only fatality in this series occurred as a result of dislodgment of a large thrombus from the left atrium immediately following operation, producing occlusion of the aorta at its bifurcation and mesenteric thrombosis. This patient had had several previous embolic episodes and autopsy revealed a large, partially organized thrombus attached to the lateral wall of the left atrium.

Most patients are allowed out of bed after the first few days and are encouraged to walk about the ward. The usual hospital stay after operation has been less than ten days.

CLINICAL EXPERIENCE

Twenty-one patients with a diagnosis of mitral stenosis have been operated upon with one fatality. According to the functional capacity rating specified by the American Heart Association, we have classified these twenty-one cases into the following categories: Class II—three cases; Class III—ten cases; Class IV—eight cases. Most of the patients in this series were severely incapacitated, and two had been totally bedfast for more than a year. One of the Class III patients was in the second trimester of her first pregnancy at the time of valvulotomy. All patients have been selected for the operation on the basis of the severity of their incapacitation and, in general, the results have been satisfactory.

SUMMARY

The technique of mitral valvulotomy employed in twenty-one consecutive patients with mitral stenosis is presented. An anterior fourth intercostal space incision with division of the fourth costal cartilage has provided satisfactory exposure. The maneuvers of introduction and withdrawal of the finger without blood loss are described briefly. Digital dissection of the commissures is the standard procedure, but on occasion a valvulotome may be necessary to initiate the division of the commissures. Closure of the auricular appendage is done with multiple interrupted sutures. The amputated auricular appendage and a lung biopsy are studied for characteristic histologic changes. The use of procaine hydrochloride as intravenous injection, pericardial instillation, or myocardial infiltration has not been found necessary. Instead, quinidine is employed to reduce the complications produced by cardiac arrhythmias.

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SOME OBSERVATIONS ON THE TREATMENT OF CARCINOMA OF THE PANCREAS*

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NOTHING exists in this world of as great importance as a man of character and accomplishment. Such a man was E. Starr Judd. His gifts were those of a master surgeon, scientist, scholar, humanitarian, and gentleman. When we honor annually such men as Dr. Judd we bequeath to coming generations our appreciation of the great contributions they have made to medicine.

The story of the treatment of carcinoma of the pancreas is not encouraging, but it is not without hope. The stimulus given to the investigation of this subject by Whipple, Parsons, and Mullins,[1] in 1935, deserves the highest praise, even though the results of the treatment they suggested may have caused some disappointment. But progress has been made and will continue to be made. Notable advances have developed gradually in the diagnosis, selection of patients suitable for the radical operation, and in operative technique.

A summary of the results of treatment of carcinoma of the pancreas at the University of Kansas covers a period of twelve years. All patients in whom a diagnosis of carcinoma of the pancreas was made are included, as shown in Table I. A total of 103 records have been studied. All patients have been traced.

Eighty-two of the 103 patients were operated upon. Of this number, twenty-four had pancreatoduodenectomies with an operative mortality of 29.1 per cent (Table II). One patient survived thirty-seven months. The average survival period was 15.2 months. The mortality rate of the one-stage operation was 26.6 per cent, and of the two-stage operation, 33.3 per cent.

There were forty palliative operations of various types for carcinoma of the ampullary region with eleven deaths, a mortality rate of 27.5 per cent (Table III). The average length of survival time was 4.4 months. One patient in the palliative list had a pancreatoduodenectomy after Dec. 31, 1951, and died postoperatively.

The results of operations upon the body and tail of the pancreas are shown in Table IV. Three patients were alive on March 20, 1952—3 months, 11 months, and 10 months, respectively, after operation. It is believed that none of these patients is cured.

DISCUSSION

There are many problems to be solved in the surgical treatment of carcinoma of the pancreas, although some important problems have already been solved. The greatest interest has centered upon the treatment of carcinomas arising from the ampullary region and head of the pancreas. Carcinomas of the body

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TABLE I. TOTAL NUMBER OF PATIENTS DIAGNOSED OR TREATED FOR CARCINOMA OF PANCREAS*

Pancreatoduodenectomy (head)	24
Palliative operations (head)	40
Exploration only (head)	1
Clinical diagnosis only (head)	13
Autopsy diagnosis only (head)	5
Excisions (body and tail)	4
Palliative operations (body and tail)	7
Exploration only (body and tail)	6
Diagnosis at autopsy (body and tail)	3
Total	103

*Jan. 1, 1940, to Dec. 31, 1951.

and tail of the pancreas do not present the difficulties that are inherent in the treatment of carcinomas of the ampullary region, since their removal does not involve any great disturbance of digestive physiology. Carcinomas of the body and tail of the pancreas are not included in this discussion.

TABLE II. RESULTS OF PANCREATODUODENECTOMY*

PATIENT	AGE	SEX	YEAR	ONE- OR TWO-STAGE	RESULTS
M. B.	67	F	1940	2	Lived 23 months
C. T.	47	M	1940	2	Lived 34 months
A. B.	59	M	1941	1	Lived 33 months
G. P.	65	F	1942	2	Lived 15 months
A. M.	72	F	1942	2	Lived 37 months
B. R.	66	M	1942	1	Lived 17 months
M. S.	56	F	1943	1	Lived 8 months
I. F.	54	M	1944	1	Lived 12 months
O. L.	39	M	1945	2	Postoperative death
H. B.	68	M	1945	2	Postoperative death
W. T.	68	F	1946	1	Lived 14 months
A. A.	66	M	1946	1	Lived 3 months
R. A.	57	M	1947	1	Postoperative death
C. G.	67	M	1947	2	Postoperative death
P. D.	70	M	1947	2	Lived 9 months
Y. T.	66	F	1947	1	Lived 6 months
J. S.	59	M	1948	1	Lived 3 months
C. W.	58	M	1948	1	Postoperative death
A. F.	78	F	1948	1	Postoperative death
E. M.	58	M	1948	1	Postoperative death
G. G.	55	M	1948	1	Lived 6 months
M. B.	60	F	1949	2	Lived 16 months
L. G.	52	M	1950	1	Lived 10 months
M. T.	53	F	1950	1	Lived 13 months

Number that survived operation	17
Number of postoperative deaths	7
Mortality from operations	29.1 per cent
Mortality from one-stage operations	26.6 per cent
Mortality from two-stage operations	33.3 per cent
Average length of postoperative survival	15.2 months

*The first 9 patients have been reported previously.[2]

Selection of Patients for Radical Pancreatoduodenectomy.—It is obvious that early diagnosis and early operation are essential to the improvement of results in the treatment of this discouraging disease. Modern methods of diagnosis make the outlook more hopeful, but much stimulation is yet needed to spur the physician, who first sees the patient, into therapeutic action. There is still too great a hiatus between symptoms and surgery.

TABLE III. PALLIATIVE OPERATIONS, CARCINOMA OF AMPULLARY REGION

Cholecystogastrostomy	5
Cholecystoduodenostomy	8
Cholecystoduodenostomy and gastrojejunostomy	2
Cholecystojejunostomy	6
Cholecystogastrostomy and gastrojejunostomy	5
Cholecystojejunostomy and jejunojejunostomy	2
Choledochoduodenostomy	3
Choledochoduodenostomy and gastrojejunostomy	1
Choledochojejunostomy	2
Choledochostomy	1
Cholecystojejunostomy, jejunojejunostomy and pancreatojejunostomy	1
Gastrojejunostomy or duodenojejunostomy (carcinoma uncinate process)	4
Total	40
Number postoperative deaths	11
Number survived operations	29
Postoperative mortality rate	27.5 per cent
Average length of postoperative survival	4.4 months

TABLE IV. CARCINOMA OF BODY AND TAIL OF PANCREAS

PROCEDURE	NUMBER OF PATIENTS	RESULTS
Body		
Excised	1	alive 3 months
Palliative operations	7	1 alive 11 months
1 postoperative death (14.3 per cent)		
length of postoperative survival (average)—8.2 months		
Exploration only	5	
1 postoperative death (20.0 per cent)		
length of life of survivors (average)—5.7 months		
Excised with gastrectomy	1	lived 4 months
Death hypernephroma found at autopsy	1	
Found at autopsy	1	
Tail		
Excised with resection of esophagus	1	postoperative death
Excised with gastrectomy	1	alive 10 months
Exploration only	1	lived 2½ months
Found at autopsy	1	
Total	20	

Selection of patients for the radical operation at the operating table may present serious difficulties. One must first decide if the obstruction of the common duct is due to carcinoma and, if a carcinoma is present, if the radical operation is justifiable. To differentiate between a benign lesion and a carcinoma of the ampullary region or head of the pancreas may tax the ingenuity and skill of the most experienced surgeon. An operation of the magnitude of pancreatoduodenectomy for a benign condition, such as chronic pancreatitis, is not indicated and may have serious consequences. The results of five such operations are shown in Table V.

TABLE V. NUMBER OF CASES OF PANCREATODUODENECTOMY FOR CARCINOMA WHICH PROVED TO BE PANCREATITIS

AUTHOR	NUMBER OF CASES	RESULTS
Probstein, Sachar, and Rindskopf[10]	1	postoperative death
Orr[2]	1	postoperative death
Cattell and Pyrtek[8]	3	1 postoperative death
Total	5	

It is generally believed that lymph node metastases and infiltration of the portal or superior mesenteric vein by carcinoma are contraindications to the radical operation. This opinion is not completely accepted by Brunschwig[3] or by Miller and Clagett[4] who have reported five-year survivals with metastases to lymph nodes. It is easy to outline with the pen the indications for and against the radical operation, but when confronted with the pathology during an operation one may find it difficult to determine the extent of the tumor. If in doubt it is probably wiser to err on the side of radicalism than to court certain disaster by palliation. Pancreatoduodenectomy is advised without hesitation if a carcinoma is found in the ampullary region without demonstrable evidence of metastases or extension of the tumor to the portal or superior mesenteric vein.

Does Radical Removal of Carcinoma of the Ampulla or Papilla Offer a Better Prognosis Than Radical Excision of Carcinoma of the Head of the Pancreas? It has been suggested that carcinomas arising in the ampulla or papilla of Vater grow slowly and metastasize late compared to those having their origin in the head of the pancreas. As early as 1913 Outerbridge[5] studied the pathology of carcinoma of the papilla of Vater and suggested that such tumors might be cured by radical operation. Further evidence that operation might cure carcinoma of the papilla has been presented by Baggenstoss,[6] who found fifteen of thirty-eight patients examined by him at autopsy without evidence of metastases.

Clinicians in general have the opinion that the results of treatment of carcinoma of the ampulla are much more favorable than treatment of carcinoma primary to the head of the pancreas. Siler and Zinninger[7] doubt that carcinomas of the ampullary region are of low-grade malignancy and metastasize late. They cite one patient in whom gross metastases developed in the liver in a seventeen-day interim between the two stages of a pancreatoduodenectomy. Cattell and Pyrtek (1949)[8] expressed great discouragement concerning treatment of carcinoma of the head of the pancreas and believed that they should modify their procedure or abandon the radical operation. It is very probable that, if a carcinoma developing in the head of the pancreas could be diagnosed as early as one at the ampulla producing jaundice, there would not be much difference in the results of operation for carcinoma in the two locations.

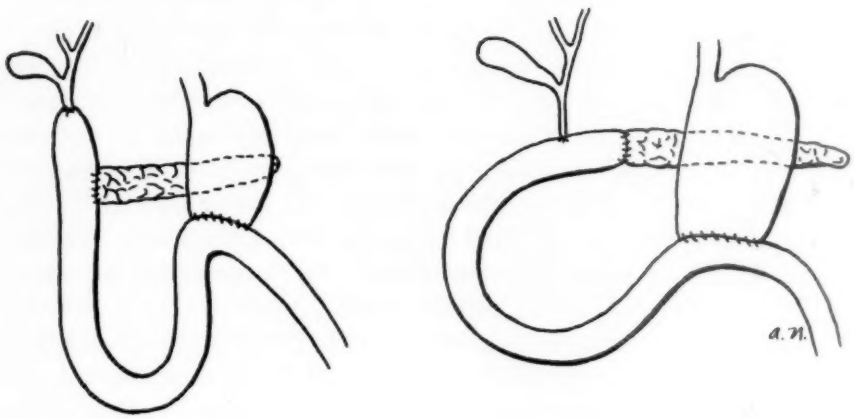
Can the Exact Origin of a Carcinoma of the Ampullary Region Always Be Determined? My experience and the recorded evidence indicate that the correct answer is no. Outerbridge stated that the exact origin of a primary carcinoma occurring in the region of the papilla of Vater usually is difficult to determine. He believed that such a differentiation is at best more or less a matter of hair-splitting and that such tumors should be considered as a unit. Baggenstoss reported that only 43 per cent of all persons have a true ampulla. He agrees with Outerbridge that identification of the actual site of origin of neoplasms in the ampullary region is extremely difficult or impossible, even after operation or necropsy, and any attempt to classify such neoplasms from the standpoint of origin would be fruitless. Brunschwig[9] observed, in his book, *The Surgery of Pancreatic Tumors,* that the terms "ampulla of Vater" and "papilla of Vater" were used loosely in surgical literature. Commenting on terminology, Siler and

Zinninger stated that from a practical standpoint the term "ampullar carcinoma," which includes periampullary carcinomas, is satisfactory. Considering the difficulties in making an accurate diagnosis of the exact origin of tumors in and about the ampulla, the term "periampullary region" to include all tumors of that area which produce jaundice would be acceptable. It is further suggested that, for purposes of description, segments of the pancreas be divided into periampullary, head, uncinate process, body, and tail. Tumors of the head of the pancreas may be far advanced before they encroach upon the common duct and produce jaundice, and tumors of the uncinate process may produce obstruction of the duodenum without evidence of jaundice. Four patients in our series had primary carcinomas of the uncinate process.

Technique of Pancreatoduodenectomy.—A careful survey is made for metastases. Any suspicious lymph node should be removed for examination. While this examination is being made the duodenum may be mobilized to determine the extent of the tumor and evidence of local extension. At this time one not infrequently is confronted with the possibility that the mass in the ampullary region may not be carcinoma. Often an accurate diagnosis cannot be made without tissue for biopsy. Every surgeon knows the shortcomings of the usual biopsy. The lesion is often too small or too deep to be reached and the danger of a pancreatic fistula must be remembered. By mobilizing the duodenum a specimen for a biopsy may sometimes be taken from the tumor. If this is not possible a specimen for biopsy taken with the Vim-Silverman needle may be helpful as suggested by Probstein and associates.[10] If there is still doubt, the duodeneum should be opened, the papillary area inspected, and a specimen for biopsy taken from any evident mass or ulceration. If carcinoma is proved and metastases are not found, a further careful estimate of operability should be made by exploring the portal and mesenteric veins, both from above and below the pancreas, to determine if the tumor has infiltrated either vein. In the absence of demonstrable metastases or infiltration of the veins, the radical operation is indicated. In carefully selected cases, pancreatoduodenectomy is advised when near-by regional lymph nodes contain metastases.

Although many techniques have been described since 1935, it is now generally agreed that the two techniques shown in Fig. 1 are most acceptable. Whipple[11] recognized early (1943) that pancreatojejunostomy is advisable to improve fat digestion and to minimize the incidence of pancreatic fistula. There is no longer any dispute concerning the advisability of anastomosing the severed end of the pancreas to the intestine. Although it is a well-known fact that patients will live without the external pancreatic secretion, re-establishing the flow of pancreatic juice into the intestine is physiologic and without as much danger of pancreatic fistula as closure of the pancreatic duct. Anastomosis of the bile duct to the intestine is preferred to anastomosis of the gall bladder since it reduces the incidence of biliary fistula. Parsons[12] recently has recommended removal of the lower common duct and anastomosis of the upper portion because of the incidence of spread of carcinoma in the walls of the lower end of the duct. The method of anastomosis between the pancreatic duct and the jejunum seems to make very little difference in the end results. The severed end of the pancreas

may be capped with the open end of the jejunum or implanted into the side of the jejunum. If either of these anastomoses is used the pancreatic duct should be visualized and splinted with a tube placed temporarily within the duct to prevent inclusion of the duct wall in sutures. The main pancreatic duct lies in the posterior half of the pancreas in the neck region. Special tubes have been used for implanting the pancreatic duct into the jejunum such as rubber tube (Varco[13]), silver tube (Poth[14]), Vitallium tube and ureteral catheter (Reynolds and Pearse,[15] Siler and Zinninger[7]). It is doubtful if any type of special tube is necessary for a successful anastomosis if care is used in implanting the severed end of the pancreas into the intestine.



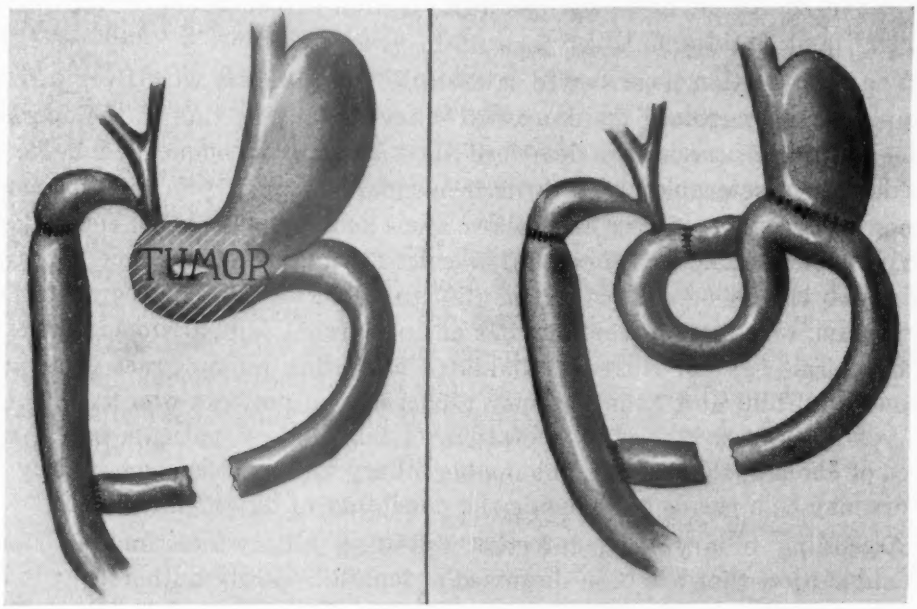
A. *B.*

Fig. 1.—Sketches of completed pancreatoduodenectomies. *A*, Redrawn and modified from Dennis. *B*, Redrawn and modified from Waugh and Clagett. The techniques shown here of choledochojejunostomy, cholecystojejunostomy, pancreatojejunostomy, and placing a long loop of jejunum proximal to the gastrojejunostomy have been emphasized by several authors.

Some doubt has been expressed about continued patency of the pancreatic duct after anastomosis. In experimental animals Person and Glenn[16] found that the stump of the severed pancreas could be implanted into the stomach without loss of the external pancreatic secretion. This work was substantiated clinically by Reynolds and Pearse who found the anastomosed pancreatic ducts patent in autopsies of two patients who died sixteen and twenty-two months, respectively, after pancreatoduodenectomy. Child and Ellis[17] have reported recently two autopsies, one of which showed an open and the other a closed pancreatic duct anastomosis. It was their opinion from the tissue study that pancreatic secretions had entered the bowel in the second case until shortly before death.

In 1938, Whipple[18] suggested the advisability of placing the gastrojejunostomy distal to the biliary and pancreatic anastomoses. Hunt's[19] technique of pancreatoduodenectomy, described in 1941, placed the gastrojejunostomy distal to these anastomoses. Dennis,[20] in 1942, advised that the gastrojejunostomy be placed 40 cm. distal to the biliary anastomosis. In 1944, Child[21] described his technique in which he advised increasing the distance between the biliary anastomosis and the gastrojejunostomy. Pearse[22] suggested a standard technique

stressing this point. In an autopsy report of two patients by Child and Ellis, in 1951, the pathologist recorded the anastomoses of the biliary tract to the jejunum, 57 and 34 cm., respectively, proximal to the gastrojejunostomy.



A. *B.*

Fig. 2.—Completed technique of the two-stage pancreatoduodenectomy using double biliary anastomoses to prevent ascending infection. *A*, first stage; *B*, second stage. (Redrawn from Child and Ellis.)

Should Pancreatoduodenectomy Be Done as a One-Stage or a Two-Stage Operation? In the report of Whipple, Parsons, and Mullins[1] in 1935, pancreatoduodenectomy was done in two stages. It was soon appreciated that the operation should be done in one stage whenever the condition of the patient was not a contraindication. Whipple[23] did the first successful one-stage pancreatoduodenectomy in March, 1940, which he reported in 1941. The same year, Hunt[19] and Trimble and associates[24] described one-stage operations. In 1943 Whipple definitely stated that he preferred the one-stage operation,[11] and in 1945 he condemned the two-stage operation and advocated a one-stage procedure with choledochojejunostomy and implantation of the pancreatic duct into the jejunum.[25] In 1949, Cattell and Pyrtek[8] expressed preference for the one-stage operation, but were definite in their opinion that the two-stage operation was advisable in some poor-risk patients and enabled them to extend the operation to patients not otherwise suitable risks for the radical operation. If the two-stage operation is chosen, Child and Ellis[17] have illustrated a double biliary anastomosis technique, as shown in Fig. 2, which may be an improvement over previously described procedures. This double anastomosis was first suggested by Brunschwig and Tiholiz[26] in 1946.

Complications of Pancreatoduodenectomy.—In addition to hazards incident to any major operative procedure there are complications which may follow this

radical operation. Pancreatic and biliary fistulas have been reported frequently. These complications may be reduced to a minimum by careful choledochojejunostomy and pancreatojejunostomy. Of the late complications peptic ulcer has been observed at or near the gastrojejunostomy stoma or in the stomach (Owens,[27] and Child and Ellis[17]).

The complication most feared is ascending cholangitis with liver infection. Whipple early recognized the danger of biliary tract infection in the operations which he and his associates described in 1935, and recommended a Roux Y procedure as preferable.[1] To further combat this infection the segment of jejunum between the biliary and gastric anastomoses should be 20 cm. or longer. In experimental animals Pearse and associates[28] found that a Roux Y antiperistaltic limb should be at least 12 in. (30 cm.) long to prevent regurgitation of dye, barium, or intestinal contents out of an external jejunal stoma. This type of anastomosis has not entirely eliminated ascending biliary tract infection, as is shown by Child and Ellis' autopsy report of two patients who lived five and four years, respectively, after operation. Each of these patients had a severe degree of cholangiohepatitis. The double biliary anastomosis suggested by these authors may be a means of reducing the possibility of biliary infection.

Ascending biliary tract infection following biliary-intestinal anastomosis is an old subject that has been discussed at length by many authors. It is interesting to note that nearly fifty years ago Montprofit[29] first used the Roux Y type of cholecystenterostomy to avoid ascending biliary infection. He also proposed that choledochojejunostomy and hepaticojejunostomy be constructed by the Roux Y technique. In 1936, Eliason and Johnson[30] reviewed this subject thoroughly and concluded that liver infection is a frequent enough complication of biliary-intestinal anastomosis to prevent its indiscriminate use. When making biliary

TABLE VI. OPERATIVE MORTALITY OF PANCREATODUODENECTOMY

AUTHOR	OPERATION	YEAR REPORTED	NUMBER OF CASES	MORTALITY RATE (PER CENT)
Whipple	1 stage	1945	19	31.0
	2 stage		8	38.0
Dennis and Varco		1946	14	29.0
Waugh and Clagett		1946	30	20.0
Waugh		1946		
Head of pancreas	1 stage		13	7.7
	2 stage		4	25.0
Ampulla	1 stage		7	28.6
	2 stage		3	33.3
Bartlett	1 stage	1947	11	45.4
	2 stage		13	23.0
Waugh		1948	43	28.0
Brunschwig	1 stage	1949	15	26.6
	2 stage		2	100.0
Cattell and Pyrtek		1949	56	14.3
Priestley et al.		1950	4	0.0
Orr	1 stage		15	26.6
	2 stage	1952	9	33.3

tract anastomoses of any kind the admonition of Wangensteen,[31] expressed in 1928, that the incidence of infection depends upon the size of the anastomotic stoma, should be kept in mind.

Results of Pancreatoduodenectomy. In the twenty-four cases of pancreatoduodenectomy at the University of Kansas, none of the patients lived longer than thirty-seven months postoperatively. The average length of survival time was 15.2 months. The operative mortality rate of pancreatoduodenectomy compiled from the publications of several authors is shown in Table VI. The published records are not complete enough to arrive at an accurate estimate of the average length of life in a large series of patients surviving pancreatoduodenectomy. Miller and associates[32] recorded their late results of pancreatoduodenectomy for carcinoma of the head of the pancreas and ampulla. Of eighteen patients operated upon for carcinoma of the head of the pancreas, thirteen were dead after an average survival period of 12 month, and five were alive with a survival time of 22.9 months. The survival time for patients with carcinoma of the ampulla averaged 18.5 months for those dead, and 38.3 months for those living.

TABLE VII. NUMBER OF PATIENTS WHO LIVED FIVE OR MORE YEARS FOLLOWING PANCREATODUODENECTOMY

AUTHOR	YEAR REPORTED	NUMBER	LOCATION	LENGTH OF LIFE
Whipple	1945	1	Islet cell of head	Lived 10 years (reported by Parsons, 1951)
Bartlett[33]	1947	1	Not stated	Living 5 years in 1947
Siler and Zinninger	1948	1	Ampulla	Lived 7 years and 3 days, died of melanoma
Cattell and Pyrtek	1949	1	Ampulla	Living 6 years and 2 months in 1949
	1949	1	Ampulla	Living 5 years and 7 months in 1949
	1949	1	Ampulla	Living 5 years and 7 months in 1949
Thompson[34]	1949	1	Ampulla	Living 7 years in 1949
Brunschwig[35]	1949	1	Ampulla	Living 8 years and 9 months Feb. 16, 1952 (personal report)
Miller and Clagett	1951	1	Head	Living 5 years in 1951
	1951	3	Papilla	All living 5 years in 1951
Moore, Sako and Thomas	1951	1	Not stated	Patient of Dennis living 6 years in 1951
Child and Ellis	1951	1	Papilla	Lived 5 years and 3 months
Senff[36]	1951	1	Head	Lived more than 5 years
Brunschwig	1952	1	Head	Living 7 years and 3 months Feb. 16, 1952 (personal report)
Varco	1952	1	Ampulla	Living 6 years and 3 months in March, 1952 (personal report)
Total		17		

We are particularly interested in long-time survivors of the radical operation. Published results are now somewhat more encouraging. In Table VII is listed the number of patients reported who have lived five or more years. One cannot say with certainty that any of the seventeen patients in this list has been cured.

The Palliative Operation for Carcinoma of the Ampullary Region.—When the radical operation is contraindicated the palliative operation is indicated to relieve the discomfort of the itching of jaundice and to improve the general

condition of the patient for the few remaining months of survival. In our series of forty cases the operative mortality rate was 27.5 per cent and the average length of survival time was 4.4 months. Mortality rates of the palliative operation reported by several authors between the years 1921 and 1952 are listed in Table VIII. These mortality rates range between 7.4 and 63.6 per cent. These authors tabulate the average length of life of survivors as ranging between 4 and 15.5 months.

TABLE VIII. RESULTS OF PALLIATIVE OPERATIONS WITH ANASTOMOSIS OF GALL BLADDER TO STOMACH OR INTESTINE

AUTHORS	YEAR REPORTED	NUMBER OF PATIENTS FOLLOWED	AVERAGE LENGTH OF LIFE AFTER OPERATION, IN MONTHS	NUMBER OF PATIENTS OPERATED UPON	OPERATIVE MORTALITY RATE (PER CENT)
Babcock[37]	1921			60	10.0
Judd and Parker[38]	1928	12	7.7	34	47.0
Leven[39]	1933	8	4.0	8	25.0
Coller and Winfield[40]	1934	19	7.2	30	26.6
Judd and Hoerner[41]	1935	94	10.2		
Oppenheimer at al.[42]	1938	17	7.0	32	41.3
Ransom[43]	1938		8.6	59	23.7
Lahey and MacKinnon[44]	1938	15			
Zollinger and Kevorkian[45]	1939	17	9.0	33	21.2
Sallick and Garlock[46]	1942	25	6.3	50	48.0
Gray and Sharpe[47]	1943	4	15.5	11	63.6
Dennis and Varco[48]	1946	14			21.0
Bartlett	1947	28			25.0
Sanders and Porter[49]	1949	30	7.0	50	8.0
Priestley et al.[50]	1950			54	7.4
Child and O'Neill[51]	1951	73	7.2	107	25.0
Orr	1952	39	4.4	40	27.5

By comparing the mortality rates and length of life of patients treated by the radical and palliative operations, respectively, it is noted that they differ very little, and the months of survival average more in the radical group than in the palliative.

Sympathectomy or celiac ganglionectomy has been suggested to relieve pain in the palliative group. The right splanchnic nerve and the right sympathetic chain were resected above the diaphragm by De Takats[52] for an extensive carcinoma of the pancreas with metastases. There was relief from pain for three weeks after operation. Ray and Console[53] believed that sympathectomy is of limited value in carcinoma of the pancreas because of the tendency of the disease to spread outside of the organ to pain-sensitive areas supplied by somatic sensory nerves. In a recent personal communication Grimson[54] stated that he has been discouraging the use of celiac ganglionectomy in abdominal malignancies for much the same reason expressed by Ray and Console. These operations have been used in four of our patients with very doubtful benefit. In two patients pain was relieved for a short time.

Should the Radical Operation for Carcinoma of the Ampullary Region Be Extended? Expressions of discouragement have been heard and read concerning pancreatoduodenectomy for carcinoma of the ampullary region and head of the pancreas when any evidence of metastases or local extension of the tumor exists.

To accept such a discouraging attitude is not consistent with progress in the treatment of removable carcinoma. On the other hand, to extend operative technique to the point that it becomes a surgical exercise is reprehensible. But there must be an element of adventure in entering any unknown realm, and when sound reasoning and good judgment are the basis for extending operative technique adverse criticism is unjustified. A disease with a mortality rate of 100 per cent without operation cannot be approached with timidity, and one should not shrink from doing radical operations when they are compatible with prolonged life without misery.

We cannot help but be impressed by some of the recently published results of pancreatoduodenectomy. Reports of seventeen patients who have survived five or more years are very encouraging. In this group a patient of Brunschwig, who had a carcinoma of the ampulla with invasion of the regional lymph nodes, was reported to me personally on Feb. 16, 1952, alive and well eight years and nine months after operation. Miller and Clagett,[4] in 1951, reviewed the history of a patient who lived more than five years after pancreatoduodenectomy for carcinoma of the head of the pancreas with regional metastases to the lymph nodes.

The finding of extension of pancreatic carcinoma into the portal or superior mesenteric vein has been considered a contraindication to the radical operation. Such a belief is supported by poor results and high mortality. But it has been proved that the superior mesenteric or portal vein can be ligated or excised without serious results. As early as 1926 Colp[55] ligated the superior mesenteric vein for pylephlebitis and the patient lived for eight weeks. Ligations of this vein for accidental wounds with recovery have been reported by Robson,[56] Wilms,[57] and Schnug.[58] Brunschwig[59] was forced to ligate both portal and superior mesenteric veins after wounding them beyond repair in a case of carcinoma of the pancreas. His patient survived 10 days. Child and his associates (1950)[60] ligated the portal vein completely and suddenly in two patients with incurable carcinomas of the stomach with survival of both patients. These authors found that 76 per cent of *Macaca mulatta* monkeys tolerated ligation of the portal vein. In doing a total pancreatectomy for carcinoma, Parsons[61] found it necessary to resect a portion of the portal or mesenteric vein. His patient lived five months. Harsha and Orr[62] ligated the superior mesenteric vein in a patient with carcinoma of the pancreas who survived 11 months. Child and coworkers[63] have recently (1952) recorded the histories of two additional patients with sudden and complete occlusion of the portal vein with survival. They also describe two patients who had pancreatoduodenectomies with resection of the portal veins as a planned procedure. Both of these patients survived the operations and were alive two months and twenty-one days, respectively, when reported. These authors add a personal report made to them by Person and Devine,[64] who successfully removed a pancreatic tumor with the portal vein in a one-stage operation.

In some of the case reports mentioned above it is believed that the portal or superior mesenteric vein was partially occluded by the tumor before ligation or resection. Since it is a well-known fact that the portal vein can be gradually

occluded and resected or ligated with relative safety, it is assumed that ligation or resection of a normal portal vein would be more dangerous than if the vein were partially obstructed by tumor.

In 1947, Schafer and Kozy[65] studied the possibility of combining pancreatoduodenectomy with portal vein resection and anastomosis of the superior mesenteric vein to the vena cava. Dogs were used for their experiments. They found that three of six dogs lived after excision of the portal vein and anastomosis of the superior mesenteric vein to the vena cava, but when pancreatoduodenectomy was done in addition to the vein excision and anastomosis, only three of twenty-two animals lived beyond the postoperative period. Moore, Sako, and Thomas[66] were successful in doing an end-to-end anastomosis of the superior mesenteric vein after resecting 3 cm. of the vein with a carcinoma of the head of the pancreas.

There is some evidence in the reports just cited that further extension of the radical operation for carcinoma of the ampullary region may be practical.

Is Pancreatoduodenectomy a Justifiable Palliative Operation? Since radical operation for incurable cancer has been used as palliative treatment in various parts of the body with prolongation of life and relief of symptoms it is reasonable to believe that pancreatoduodenectomy may be a logical treatment in selected patients who are obviously incurable. A summary of over 1,000 patients treated by palliative procedures was made by Child and co-workers in which the average length of life of patients who survived operation was 7.5 months. By comparison these authors found that the average survival time of thirteen patients treated by pancreatoduodenectomy was fifteen months. In my own series the average survival time of patients treated with palliative operations was 4.4 months compared with 15.2 months survival period for those patients having pancreatoduodenectomies.

To date the mortality rate of pancreatoduodenectomy compares favorably with that of the palliative operation (Tables VI and VIII) and recent reports indicate that the mortality rate of the radical operation, which heretofore has been between 20 and 30 per cent, is being reduced below 10 per cent (Parsons,[12] Waugh,[67] and Cattell and Pyrtek[8]).

The published evidence that the mortality rate of pancreatoduodenectomy is no greater than that of the palliative operation, that the mortality rate of the radical operation is being reduced, and that life is prolonged by the radical operation supports my belief that pancreatoduodenectomy is justifiable as a palliative operation in well-selected cases.

CONCLUSIONS

To date, a cure of a carcinoma of the ampullary region or head of the pancreas has not been recorded regardless of the method of treatment. Reports of seventeen patients who have had pancreatoduodenectomies and lived five or more years have been collected.

The mortality rate of pancreatoduodenectomy is being reduced gradually by careful selection of patients, by improvements in technique, and by better preoperative and postoperative care.

Experienced surgeons agree that the one-stage pancreatoduodenectomy is advisable when the condition of the patient is not a definite contraindication, and that the two-stage operation should be used only in the poor-risk patient.

The effect upon the mortality and length-of-life rate of extending the radical operation is yet to be determined. To discourage extension of the operation would be contrary to sound principles of cancer surgery.

Further reports of final results of the operative treatment of carcinoma of the pancreas should be encouraged.

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A METHOD TO IMPROVE ROENTGEN DIAGNOSIS OF BILIARY DISEASES WITH BILE ACIDS

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ON SEVERAL occasions we have observed that although a preliminary cholecystogram failed to visualize the gall bladder in a patient suspected of cholecystitis, a subsequent picture after the patient received bile acids for several days either changed the diagnosis or definitely confirmed it. At least one author has used bile acids diagnostically as well as therapeutically.[1] Still, the diagnostic value seems little enough realized to render it worth recording.

PHYSIOLOGIC CONSIDERATIONS

The ability of the gall bladder to receive and concentrate radiopaque material for cholecystogram is a useful test of gall bladder function. Tetraiodophenolphthalein, used in the original Graham-Cole test, is selectively secreted by the liver and is opaque to roentgen rays when concentrated in the proper amounts. The gall bladder can concentrate the bile containing the dye as much as ten times, since it absorbs the water and inorganic salts. The failure of the gall bladder to visualize can, therefore, be interpreted as denoting the presence of biliary tract disease.

Causes for the nonvisualized gall bladder can be grouped as follows: (1) Failure of the absorption of the dye from the intestinal tract into the liver. The unabsorbed contrast media can be seen in the gastrointestinal tract on the roentgenogram. In a repeat cholecystogram there may be complete absorption. (2) Liver diseases resulting in deficient secretion of bile such as in cirrhosis, chronic passive congestion, and tumor. The hydrocholeretic action of bile acids usually can overcome this deficiency. (3) Obstruction, partial or complete, of the cystic duct preventing dye from entering the gall bladder. This may be due to edema, inflammation, or stone, or all three. (4) Improper administration of the radiopaque material. (5) Congenital absence of the gall bladder. (6) Stasis in the gall bladder which causes the majority of nonvisualized gall bladders.

Stasis may be either primary or secondary to diseases of the gall bladder, liver, and pancreas. Primary stasis is believed to be due to our highly civilized way of life with its nervous tension, premasticated foods, and undigested diets.[2] It is common knowledge that the elimination of cholagogic foods is quite frequent in our modern diet because of the widely disseminated concept

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that greasy, fried foods are harmful. Unpleasant experiences resulting from ingestion of these foods in the dyspeptic individual also influence others. The resultant biliary stasis, which prevents the radiopaque material from concentrating in the gall bladder, is also the precursor for cholecystitis and cholelithiasis.

The most common cause for nonvisualization of the normal gall bladder is biliary stasis. In stasis there is not the free exchange of bile normally present between the gall bladder and the hepatic duct. The contrast medium cannot enter the gall bladder in sufficient amounts to be radiopaque.

Many of these nonvisualized gall bladders can be made visible by relieving this stasis, thereby permitting the dye to enter the gall bladder. If there is then enough normal gall bladder function to concentrate the dye, there will be roentgen visualization. After relieving this stasis, visualization of the gall bladder may often demonstrate nonradiopaque cholesterol stones as shadows within the dye which previously were not seen. If a roentgen normal-appearing gall bladder is seen, then this suggests that liver or pancreatic disease may be responsible for the symptoms. If the gall bladder continues to be nonvisualized, then it is probable that the gall bladder is severely diseased and cannot function.

There are many ways in which biliary stasis can be relieved. In our experience the use of bile acids has been very satisfactory. Bile acids have a hydrocholeretic action, that of increasing the flow and thinning the bile. When given over a sufficient period of time they will flush out the entire biliary tract including the gall bladder. They do not cause contractions of the gall bladder. This is advantageous in that when administered in face of gall bladder disease there is no pain resulting. The administration of a fatty meal for several days prior to cholecystogram has been recommended by Curl[3] and others. Sosman,[4] however, has found that this tends to precipitate the dye and prevent its absorption. This is particularly true when a fatty meal is given just preceding the administration of the dye. He believes that the fatty acids and tetraiodophenolphthalein combine to form an insoluble compound. The fatty meal has the further disadvantage of causing contractions of the gall bladder which may precipitate an acute exacerbation of chronic cholecystitis. The only contraindication to the use of bile acids is complete obstruction of the common duct which will manifest itself by jaundice and acholic stools.

CLINICAL OBSERVATIONS

Ten patients who received a double dose of iodoalphionic acid (Priodax) and still had nonvisualization of the gall bladder were treated with bile acids (Decholin or Ketochol) from five to thirty-two days (Table I). The double dose cholecystogram was then repeated. In seven patients concentration of the radiopaque material was then sufficient for roentgen diagnosis. Two of these were eventually diagnosed as pancreatitis, one of which was proved to have a normal gall bladder at surgery when a sphincterotomy was performed.

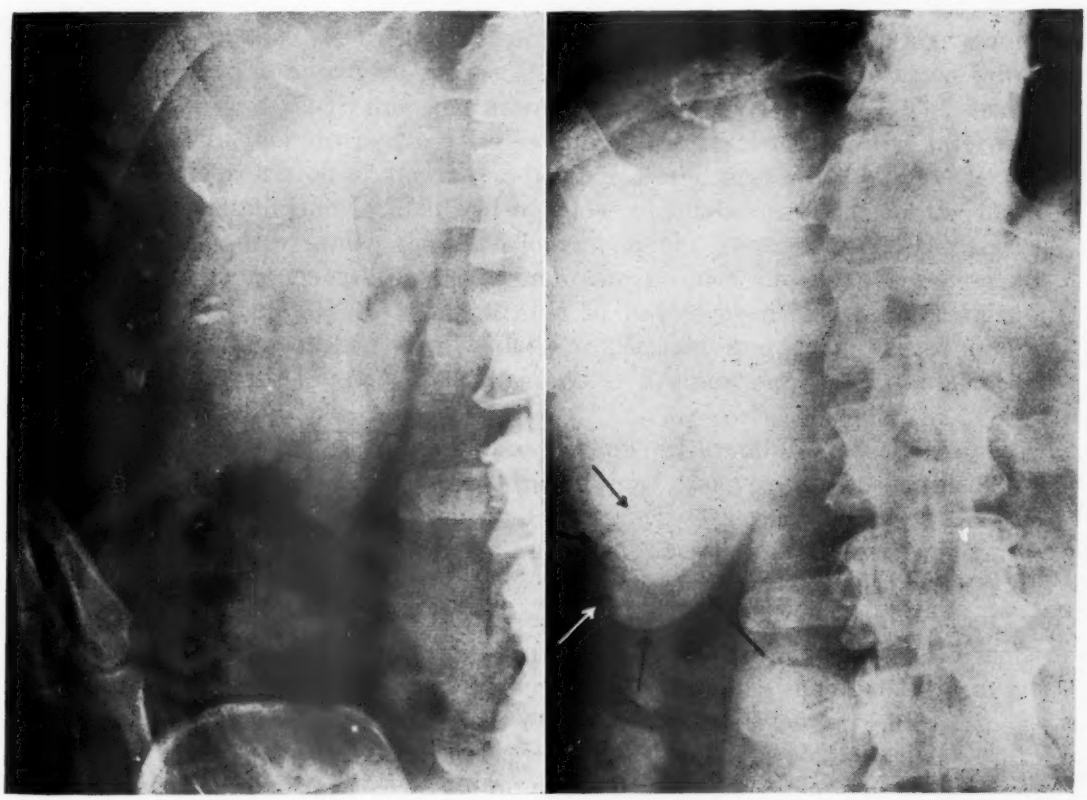
TABLE I. RESULTS OF BILE ACID THERAPY IN TEN PATIENTS WHOSE CHOLECYSTOGRAMS FAILED TO VISUALIZE AFTER SINGLE AND DOUBLE DOSES OF IODOALPHIONIC ACID CONTRAST MEDIUM

PATIENT	MEDICATION	REPEAT DOUBLE DOSE CHOLECYSTOGRAM	FINAL DIAGNOSIS AND COURSE
1. M. C.	Decholin, 2 tablets three times a day for five days	Normal visualization	Chronic pancreatitis. At surgery normal gall bladder found and sphincterotomy performed.
2. A. S.	Ketochol, 2 tablets three times a day for five days	Normal visualization	Chronic pancreatitis.
3. L. T.	Ketochol, 2 tablets three times a day for seven days	Poor visualization	Probable mild to moderate cholecystitis; discharged to be followed in the clinic.
4. G. B.	Ketochol, 2 tablets three times a day for thirty-two days	Poor visualization	Probable mild to moderate cholecystitis; discharged to be followed in the clinic.
5. E. R.	Decholin, 2 tablets three times a day for nine days	Visualized with numerous radiolucent stones	Numerous cholesterol stones found at surgery—cholecystectomy.
6. J. H.	Decholin, 2 tablets three times a day for eighteen days	Normal visualization	Chronic hepatitis.
7. C. H.	Ketochol, 2 tablets three times a day for seven days	Nonvisualization	At surgery, severe cholecystitis with ulceration and arteritis.
8. R. R.	Decholin, 3 tablets three times a day for ten days	Nonvisualization	At operation, a fibrotic gall bladder containing numerous cholesterol stones.
9. L. H.	Ketochol, 2 tablets three times a day for seven days	Visualized with numerous radiolucent stones	At surgery, chronic cholecystitis with numerous cholesterol stones.
10. W. F.	Ketochol, 2 tablets three times a day for fourteen days	Nonvisualization	At surgery, a chronic purulent cholecystitis with giant cell reaction and incarcerated stones tightly packed.

One case was subsequently diagnosed as hepatitis. In two patients numerous radiolucent stones could be seen within the concentrated dye, and cholesterol stones were found at surgery (Fig. 1). In two patients poorly visualized gall bladders were seen, and, as symptoms had subsided rapidly, they were discharged to the clinic. It is felt that they probably have a mild to moderate cholecystitis, with impaired cholecystic function. In the three cases that failed to visualize following a course of bile acids, at surgery one patient was found to have severe cholecystitis with arteritis and ulceration of the gall bladder. The second patient was found to have a fibrotic gall bladder containing numerous chloesterol stones which were also present in the common duct. The third patient had incarcerated stones packed tightly in a chronic purulent cholecystitis with giant cell reaction. Obviously these last three patients had such severe biliary disease that the gall bladder could not function. The above cases illustrate the usefulness of bile acids as a diagnostic agent in biliary tract diseases.

Since a so-called single dose of iodoalphionic acid (Priodax) sometimes fails to be visualized, a subsequent double dose might be visualized. The repeat double dose cholecystogram eliminates the possibility that the con-

trast media was insufficient, or that the technique was faulty when the gall bladder persisted in remaining nonvisualized. For this preliminary report we adopted the procedure of giving bile acids (Decholin or Ketochol), two tablets before each meal, for eight to ten days after a double dose Priodax nonvisualized gall bladder was obtained. As we have had no discomforts or reactions of any kind with double dose iodoalphionic acid (12 tablets), we have begun to eliminate the single dose. Eight to ten days were chosen, as that was felt to be sufficient time to overcome stasis in the biliary tract unless the gall bladder was badly diseased. Perhaps eventually bile acids may be given eight to ten days prior to the initial cholecystogram in order to save time and the need for possible additional roentgen gall bladder studies. It is also advisable that the bile acids be discontinued on the day of the cholecystogram.



A. *B.*

Fig. 1.—Patient E. R. (Case 5 in Table I.) *A*, First cholecystogram in which gall bladder is not visualized. *B*, Cholecystogram obtained after taking bile acids three times a day for nine days. The gall bladder is visualized with numerous radiolucent stones.

SUMMARY

The nonvisualized gall bladder is discussed. The use of bile acids as a diagnostic adjunct to the cholecystogram is presented. The bile acids relieve the biliary stasis which is frequently the cause of nonvisualization of the gall bladder. The repeat cholecystogram may show nonradiopaque stones demonstrable

within the radiopaque dye. If normal, it suggests liver or pancreatic disease as a cause of the symptoms. If the gall bladder persists in remaining nonvisualized, severe gall bladder disease is probable.

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A METHOD OF REPAIR OF THE VERTICALLY DIVIDED STERNUM

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THE degree of morbidity following the vertical division of the sternum in exploration of the mediastinum depends largely upon the stability of the bony fragments after repair. Immobilization of the sternum, especially after the super-radical operation of Wangensteen for carcinoma of the breast, is difficult to obtain. In this operation the sternum is divided from above downward as far as the fourth interspace. The sternal knife is then directed toward the diseased side separating the sternum into two fragments. The smaller fragment is further divided by transection at the level of the first intercostal space. After resection of the major portion of the first rib, the clavicle with half of the manubrium is mobilized to allow adequate dissection of the neurovascular structures under the clavicle and at the root of the neck.[2] Firm fixation of the fragments of the manubrium is most important because any motion at this point of division, turning in bed or even breathing, results in severe pain. Since postoperative deep respiration and cough are therefore markedly suppressed, larger doses of narcotics are necessary, and complications are more likely to occur.

Cope[1] recommended repair of the sternum with stainless steel wire which has sufficient tensile strength to be drawn tight and yet can be handled with ease. Steel wire passed through drill holes near the margins of the sternal fragments may break, work loose, or pull out. The body of the sternum can be immobilized better with steel wire than can the manubrium, because there is less stress on the former than on the latter. For fixation of the manubrium, we have used a stainless steel tibial fixation bolt $\frac{3}{32}$ inch in diameter and 5 inches in length with a trocar point.* This bolt has a one-fourth inch fixed nut at one end and two mobile nuts of the same diameter. The washers are heart shaped with eccentrically placed holes. They are easily constructed in the hospital machine shop. (See Fig. 1 inset for measurements.) A one-fourth inch nut driver is necessary for placing the bolt and tightening the nuts.

For repairing the vertically divided sternum, drill holes are placed in each half of the body of the sternum one centimeter from the margins and at the level of the costal cartilages. One drill hole is made through the free fragment of the manubrium. No. 24 stainless steel wire is threaded through these holes. One strand of wire is passed through the drill hole in the free fragment of the manubrium and the upper drill hole in the free fragment of the body of the sternum. A strand of wire of the same size is passed about the sternum in

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*Manufactured by Zimmer Manufacturing Company, Warsaw, Ind.

each of the second and third interspaces (Fig. 1). These wires should be placed before, and not tied until after, the insertion of the tibial bolt through the manubrium.

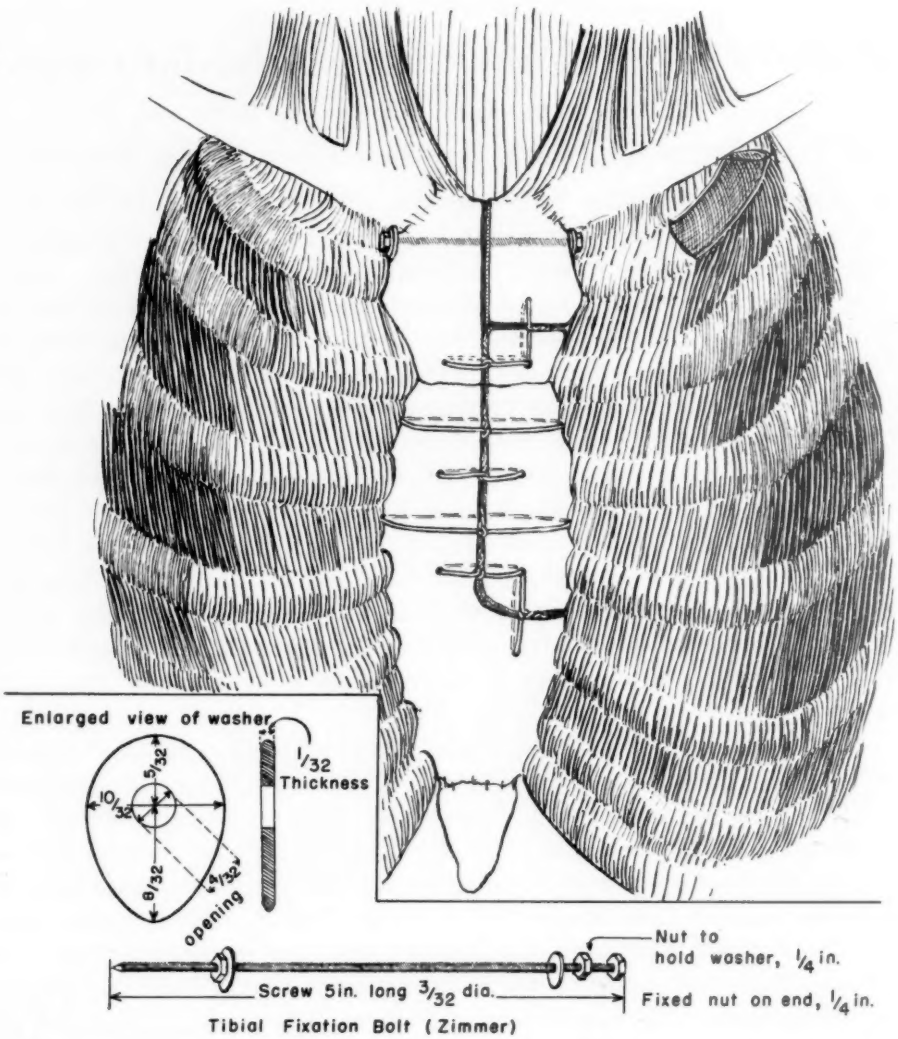

Fig. 1.—Schematic illustration of the repair of the vertically divided sternum.

In the fixation of the manubrium, the assistant maintains accurate reduction of the fragments. The surgeon depresses the point of the tibial bolt between the medial end of the clavicle and the first rib, partially displacing the costoclavicular ligament posteriorly. The bolt then is passed transversely at an equidistance between the cortices of one fragment of the manubrium until it traverses the other fragment and emerges between the clavicle and first rib on the opposite side. The washers are placed with their bases toward the skin and their apices depressed through the costoclavicular ligaments. The excess length of bolt is removed and the nuts tightened to the desired tension. This firmly fixes the manubrium. The wires are tied or twisted approximating the other

fragments. After the excess wire has been removed, the remaining wire points are carefully turned down and depressed to prevent protrusion through the skin at a later date.

When the sternum has been divided longitudinally without multiple transection of either half, two fixation bolts may be used alone for repair without additional use of steel wire. The first should pass through the manubrium as described and the second through the body of the sternum at the level of the second or third interspace.

SUMMARY

A satisfactory method of repair of the surgically divided sternum is described using a tibial fixation bolt and steel wire.

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LONG-ACTING BILATERAL INTERCOSTAL NERVE BLOCK FOR UPPER ABDOMINAL SURGERY

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THE method of bilateral intercostal nerve block for upper abdominal surgery was originated and introduced by one of us (R. W. B.[1]) in 1940 because of dissatisfaction with the methods of anesthesia then available for certain seriously ill or markedly debilitated patients requiring upper abdominal surgery. It was found possible to obtain complete anesthesia of the anterior and lateral abdominal wall, including the parietal peritoneum, from the costal margin to approximately two inches below the umbilicus, by blocking the sixth through the eleventh intercostal nerves bilaterally in the midaxillary line so that their lateral branches would be included along with their anterior branches.

Inasmuch as some sensation from the visceral peritoneum is mediated by way of the splanchnic nerves, a very light supplementary general anesthesia is given in conjunction with the nerve block in order that during the intra-abdominal part of the operation the ordinary packing off and handling of intestines may be performed without discomfort to the patient. The light general anesthesia is begun before the intercostal block is performed in order to render it painless. Blocking the nerves in the midaxillary line paralyzes the rectus muscles, the lateral flat abdominal muscles, and the periphery of the diaphragm. Consequently, the tendency toward evisceration with straining, as occurs during marked respiratory efforts or vomiting, is minimized. This widespread paralysis of the abdominal musculature also permits easy and accurate closure of the abdominal wound by virtue of the complete relaxation obtained. Another very important aspect of this form of anesthesia is the brevity of the period of recovery from the general anesthesia; complete reaction usually has been attained before the dressing is applied.

It is apparent, therefore, that by means of a simple method of anesthesia we are able to enjoy the advantages of a full ether or spinal anesthesia in seriously ill individuals presenting contraindications to those methods.

In 1941, experiments were begun by R. W. B., and likewise by Zollinger,[2] employing long-acting anesthetic agents for intercostal block which were for the most part oily solutions. This was done on the theory that a great decrease or absence of incisional pain in the immediate postoperative period would decrease the splinting of the diaphragm and limitation of respiratory excursion so that fewer postoperative pulmonary complications would occur.

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A few years later, when the benefits of early ambulation became apparent to everyone, it was recognized that a relatively painless wound also would permit almost immediate and relatively free mobilization of the patient.

The original long-acting oily solutions available to us did not permit ready diffusion of the anesthetic agent so that the postoperative abdominal wall anesthesia was spotty and the results inconstant, but in the occasional cases where an accurate "hit" of most of the intercostal nerves had been obtained, the results were extremely gratifying, both to the patient and the surgeon. During this period of study we made pre- and postoperative determinations of the vital capacity, as measured by the spirometer, and found that there was little decrease in the immediate postoperative period in the favorable cases, but that the expected decrease of vital capacity in excess of 50 per cent occurred in those cases in which inadequate anesthesia was obtained. This latter situation occurs with regularity in cases in which the operation is performed under conventional methods of anesthesia.

In 1944 and 1945, Belinkoff[3, 4] reported a rather satisfactory experience with Novest-Oil which, however, was employed as an intercostal block for postoperative pain relief after a spinal or deep general anesthetic had been administered for the actual surgery.

Rather recently a new long-acting anesthetic solution, Efocaine,* having the following characteristics and mode of action, has come to our attention: A solution of anesthetic agents which are normally insoluble in water is made in a nontoxic organic solvent base. The agents used are procaine and butyl aminobenzoate. The organic solvent employed is composed of polyethylene, glycol 300, and propylene glycol. The addition of minimal amounts of water or body fluids to this solution causes a precipitation of the anesthetic agents at the site of injection. The slow reabsorption of procaine and aminobenzoate from the site of injection produces the prolonged local anesthetic action.

The possible complications due to this drug include local tissue irritation which has been shown by Weinberg[5] to be minimal. Intravascular injection of the drug may produce the same reaction as injection of procaine.

Other investigators have performed their surgery under conventional methods of anesthesia, then, at the conclusion of the operation, and with the patient still anesthetized, have carried out the intercostal nerve block with Efocaine. We feel, however, that the patient is missing a considerable part of the benefit if he does not receive the actual surgery under the intercostal block itself.

The technique of block, as originally outlined,[1] has been modified but little during the past twelve years and will be reviewed briefly. The patient is placed on the operating table with both arms abducted on boards, following which light Pentothal Sodium and N_2O in combination or light cyclopropane is induced.

The skin of the lateral chest wall is suitably prepared bilaterally. Then the surgeon or the physician-anesthetist, having donned a pair of sterile gloves,

*Manufactured by E. Fougera and Company, Inc.. New York, N. Y.

carries out the block, employing a standard 10 c.c. syringe and a No. 18 caliber needle with a point sufficiently blunt so that its passage through a fascia layer can be appreciated. The syringe is filled from the rubber-stoppered 20 c.c. bottle of Efocaine solution; then the sixth through the eleventh intercostal nerves are blocked bilaterally in the midaxillary line. The lower border of a rib is palpated, and the needle is passed through the skin and fat down to it. Following this, the needle is allowed to slip off the lower border of the rib and, in so doing, it is easily felt to pass through the fascia covering the external intercostal muscle. The direction of the needle is slightly upward into the groove beneath the rib. The point of the needle now lies between the two intercostal muscles where the intercostal vessels and nerve are situated. After the plunger has been drawn back to prevent intravascular injection, a deposit of between 1 and 1½ c.c. of the anesthetic solution is made. With this dosage seldom has there been local pain postoperatively at the site of injection as invariably occurred in our earliest cases when a 3 c.c. dosage was employed. This discomfort lasted for periods up to a month and was due, we believe, to mechanical irritation during respiration by the small bolus of precipitated procaine crystals. If one person performs the bilateral block, about the same time is required as for administering a spinal anesthesia; however, if two persons each do a side simultaneously, a matter of only two or three minutes is involved in the procedure.

As mentioned earlier, splendid relaxation of the upper abdominal muscles is present by the time the skin and fat have been incised, so that excellent exposure of deep structures, such as the common duct, is easily obtained; likewise, accurate closure of the wound is possible in such a subject. If, occasionally, a patient pushes intestines into the wound, it means that the general anesthesia is so light that he is feeling pain due to packing or handling of the visceral peritoneum. The pushing is probably due to the action of the lower abdominal musculature plus the diaphragm. This situation can be corrected in thirty seconds by the injection of an additional small amount of Pentothal Sodium.

The method is employed not only for intraperitoneal upper abdominal operations, but is also equally useful for operations on the anterior abdominal wall, such as closure of transverse colon colostomy and repair of umbilical and incisional hernias.

The following operations were performed in this series: radical subtotal gastrectomy (8), exploratory laparotomy, usually for inoperable cancer (6), gastrostomy (5), cholecystectomy (3), exploration of common duct (3), incisional herniorrhaphy (2), umbilical herniorrhaphy (2), splenectomy (2), closure transverse colostomy (2), thoracoabdominal exploration (1), colectomy splenic flexure (1), vagotomy (1), secondary excision cystic duct stump (1), closure acute perforation duodenal ulcer (1).

Excluding irrelevant conditions, such as a drug rash and subcutaneous fluid collection, the only postoperative complication was a bilateral pneumo-

thorax due to an experimental technical error on our part; the situation, however, was quickly corrected by appropriate measures and did not prolong the convalescence of this patient.

There was one postoperative hospital death occurring on the ward service in the series of 38 cases, most of which were of the very major type normally gravitating to a university hospital. This elderly patient had pre- and postoperative auricular fibrillation and died of acute cardiac decompensation one week after gastrectomy.

Under this plan of anesthesia, the patient is awake at, or shortly following, the conclusion of surgery. He is able to perform deep breathing and to cough voluntarily without undue discomfort. He is much more active in turning in the bed during the first few hours after leaving the operating room and is able to get up out of bed the evening of operation or the following morning, thus obtaining the many benefits resulting from early ambulation. In the region of the wound, hypesthesia or anesthesia to pinprick lasts for a period of one to two weeks following operation. It must be remembered that so-called "gas pains," sometimes occurring about the second postoperative day, must be differentiated from incisional pain.

It has been interesting to observe the marked decrease in the number of postoperative morphine injections which have been required in the 38 major cases in which this method was used and concerning which no special instructions or information had been given to the nursing staff. It was common for patients, such as those having gastric resections or explorations of the common duct, to require either no hypodermics or else only one or two in the entire postoperative period. When morphine was given, in many instances it was administered for general discomfort or restlessness rather than for true wound pain. The nursing staff has now been instructed to administer morphine only when the patient complains of true pain, and it is already apparent that few injections are required. This will make for a more active and alert patient. Furthermore, the patient who is physically able to help himself in the early postoperative period requires much less nursing care, thus lightening the burden on an ever overworked nursing staff. As an illustration of how well patients progress under this regime, our analysis shows that the radical subtotal gastric resections in the group of private patients (R. W. B.) were discharged from the hospital on an average of 9.3 postoperative days.

It is probable as time goes on that there will be continual improvement in the long-acting anesthetic solutions available, but it is our belief that present experience conclusively demonstrates the many advantages of the method of intercostal block. If one has any doubts about the matter, they are quickly dispelled when he asks a patient to compare his current hospital experience with one which occurred several years ago.

SUMMARY

The method of bilateral intercostal nerve block was originated and introduced by one of us (R. W. B.) in 1940 for making safer upper abdominal surgery in seriously ill patients. Experiments have been carried on since 1941

with long-acting anesthetic solutions, but none have been satisfactory until the recent advent of Efocaine, which provides seven to fourteen days anesthesia or hypesthesia of the incision. This peripheral block in combination with light Pentothal Sodium and N_2O or light cyclopropane produces surgical relaxation the equal of spinal anesthesia; the patient is awake at the conclusion of the operation; postoperative atelectasis and pneumonia are largely avoided since free respiration plus coughing are possible; hernia or eventration seldom occurs; ambulation is almost immediate; little morphine is required; and nursing care is markedly decreased.

Since instructing the nursing staff that morphine should be given for pain, but not for restlessness, only one of the last eight patients has received a hypodermic postoperatively, and this consisted of a single injection of morphine gr. $\frac{1}{6}$.

The method adds greatly to the safety and comfort of the patient.

ADDENDUM

Since the original manuscript was submitted for publication, in 15 of the last 20 cases no opiate was administered postoperatively. In 3 of the remaining 5 cases, a single injection of morphine (1/6 gr.) was given by hospital personnel for complaints, such as backache, which were in no way related to the incision.

By including the twelth thoracic nerves in the usual block, we have recently extended with considerable satisfaction the field of operation to the lower abdomen and pelvis. As our experience with this latter phase of the problem increases, an additional report will be forthcoming.

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AN ANALYSIS OF ONE HUNDRED CONSECUTIVE LUMBAR MYELOGRAMS FOLLOWED BY DISC OPERATIONS FOR RELIEF OF LOW-BACK PAIN AND SCIATICA

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RECENTLY, two of us (Key and Ford[1]) reported an evaluation of 253 lumbar myelograms followed by surgery of the lumbosacral canal in 206 of the patients. In that series, the myelogram was found to have an accuracy of about 75 per cent. Prior to 1946, we did not use myelograms because we felt that we were able to diagnose and localize lesions of discs in the lumbosacral region with a fair degree of accuracy. However, in September, 1946, we began performing lumbar myelograms in selected cases, maintaining a critical attitude as to the value of the procedure in each case.

Begg, Falconer, and McGeorge[2] have analyzed very thoroughly a series of 100 cases in which operations for disc lesions in the low back were performed. They found an accuracy of the myelogram of 85 per cent. Other series have varied from 67 to 92 per cent in accuracy (Camp,[3] Soule and associates,[4] Scoville and associates[5]).

After completing our study of 253 myelograms, we decided to continue our appraisal of the procedure and, in addition, to analyze certain points in the history and physical examination. Accordingly, in June, 1949, we began analyzing the history, physical examination, and myelographic and operative findings of 100 consecutive patients at Barnes Hospital who had myelograms followed by disc surgery. The last patient in the series was operated upon in August, 1950. All patients were on the orthopedic service at Barnes Hospital and one of us either operated upon or assisted at the operation of each patient. Both ward and private patients were included.

In patients who complain of low-back pain, with or without sciatica, we first use conservative treatment with the expectation that the symptoms will subside. Whether this is carried out in the hospital or in the office and at home depends upon the severity of symptoms and the wishes and economic condition of the patient. If the symptoms are relatively mild and the disability slight, conservative treatment may be continued for months or even years unless the patient recovers or seeks relief elsewhere.

In those cases of disc rupture with marked symptoms and disability which fail to respond with adequate relief in three to six weeks, surgery for removal of the ruptured disc is considered and usually recommended. It is at this time that we decide whether or not to subject the patient to a myelogram.

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Except in rare medicolegal cases, a myelogram should not be carried out unless surgery is definitely in prospect, because exact location of the disc lesion is of no value in the conservative treatment of the condition. We do not think that every patient to be operated upon for a possible disc lesion must have a myelogram, and do not hesitate to explore the lumbosacral canal without the aid of myelography. As a matter of fact, we perform myelograms on only about half of the patients operated upon for disc lesions in the lumbosacral area. All patients have a careful clinical study, including roentgenograms of the lumbosacral spine, but are not routinely subjected to lumbar punctures.

Of the 100 patients in this series who had both myelography and disc surgery there were 65 men and 35 women. The average age was 44 years for the men and 41 years for the women. Two of the patients were Negroes, which is about average since in the Negro race we rarely see patients with disc lesions requiring surgery.

Of the 100 patients here reported, pathologic discs were found at operation in 96 patients and only normal discs in 4 patients. In reviewing the histories of the entire group it was found that only one patient had pure sciatica without back pain. Eight patients of the 100, however, were operated upon for back pain only, no sciatica being present. In spite of the sciatica present in 92 patients, only 54 of this group complained of numbness or tingling in the affected leg. Cough and sneeze effect was found to be present in 77 of the 100 patients. Of the 4 patients with negative operative findings, 3 noted no cough and sneeze effect.

We have stated previously that many of our patients have consulted osteopaths or chiropractors and obtained manipulation of the back with varying degrees of temporary relief. It was surprising to find that only 13 of these 100 patients admitted having had their backs manipulated elsewhere prior to entering the hospital.

Of the 92 patients who complained of sciatica, it was found that in 16 cases the sciatica was bilateral. The distribution of right and left sciatica was approximately equal, 40 patients having right and 36 having left sciatica. Only 5 of the 16 patients with bilateral sciatica were found to have midline disc ruptures.

On inspection of the patient with a ruptured disc having severe symptoms, the presence of a list or sciatic scoliosis may be one of the most obvious findings. A list was present in 36 of the 100 patients. It was away from the affected side in 22 cases and toward the affected side in 14 cases. No list was present, in the 4 patients with negative exploration. A list was not present, however, in the remaining 60 patients who had positive operative findings.

All patients were examined for sensory changes, but abnormal findings consisting of hypesthesia in the distribution of the sciatic nerve were present in only 41 of the 100 patients.

In none of the 4 patients with negative operative findings were sensory changes present. Neither were changes in either the ankle jerk or knee jerk present in these 4 patients. Forty-nine of the 96 patients operated upon showed changes in either one or both of these reflexes. We do not believe that failure to find sensory changes or reflex changes is a contraindication to surgery. In our opinion, the single most diagnostic physical finding in a patient with a ruptured disc is a positive straight leg-raising test, or Lasègue test. This was present in 91 of the 96 patients with abnormal discs and in all of the 4 patients in whom normal discs were found.

We have felt that palpation of the lumbar interspaces for tenderness was a moderately accurate means of localizing a disc lesion. While tenderness in this area was present in 88 patients, in only 45 of the 96 patients with positive operative findings was this found to be an accurate localizing sign.

Although 12 of the 100 myelograms in this series were interpreted as negative, we elected to proceed with surgery in all cases. In 3 of these negative myelograms, the myelogram was accurate as the findings at operation were also negative. In 9 of the negative myelograms, pathologic discs were found. In one patient with a defect noted in the myelogram, no abnormal disc was found.

Of the 88 positive myelograms in the series, there were 19 patients in whom the defects were slight, consisting either of obliterated root sleeves or small indentations in the dural sac. Forty-seven patients had definite unilateral indentations, there were 20 midline or hourglass deformities, and 2 patients had such large ruptures that complete blocks were present.

In our first reported series we used from 3 to 17 c.c. of Pantopaque for myelography but, on account of the high incidence of reactions, we have ceased using large amounts, and for each case in this series only 3 c.c. or one ampule was used. Of the total of 300 c.c. of Pantopaque injected in these 100 patients, we were able to recover 233 c.c. Only 3 of the patients developed reactions following myelography. This is less than the reaction rate of 6 per cent which we reported in our first series of myelograms.

The average spinal fluid protein in the patients with positive operative findings was 58 mg. per cent. There was a low of 16 mg. per cent and a high of 171 mg. per cent. In 37 of the patients with pathologic discs, however, the spinal fluid protein was normal, that is, less than 50 mg. per cent. In each of the 4 patients with negative findings, the spinal fluid protein was normal.

There were 11 cases in the series in which the decision to operate was based solely on the myelogram. In these instances, the clinical findings were equivocal, and positive myelographic findings precipitated the disc operation. Of these 11 cases, operative findings were negative in 1, while in 7 patients bulging discs were found, protruded discs were present in 2, and 1 inspissated disc was found.

In the remaining 89 cases we would have proceeded with surgery regardless of the myelographic findings but hoped that the myelogram would give aid as to the exact level of the lesion.

We found no instance of intraspinal tumor in this series of cases, either at myelography or surgery.

The term extruded disc refers to one in which the nuclear cartilage lies free in the spinal canal, while a protruded disc is one in which the annulus fibrosus is no longer intact, but the nuclear cartilage is covered by intact posterior longitudinal ligament. A bulging disc is one which bulges posteriorly an abnormal amount and in which the annulus fibrosus, while degenerated and relaxed, is intact. A soft disc is one which has much less tension than normal, contains degenerated nuclear cartilage, and in which 2 c.c. or more of saline or novocaine solution can be injected. An inspissated disc is a scarred disc at a collapsed disc space and the dura and nerve root may be adherent to the floor of the canal.

In these 100 operative cases, 147 disc spaces in the lumbosacral area were explored. There were 30 discs which were considered to be normal and not removed. This leaves 117 discs which were believed to be pathologic and were removed in 96 patients. One patient with 3 bulging discs had all removed and the postoperative result has been good. In 19 patients 2 discs were removed and in the remaining 76 patients 1 disc only was excised. In the 4 negative operative cases no disc was removed.

Of the pathologic discs removed, 17 were extruded, 16 were protruded, 72 were bulging, 7 were soft, 4 were inspissated, and in one patient a large bony projection was found and removed. One pathologic disc was removed from the first lumbar interspace, 9 from third lumbar interspaces, 53 from fourth lumbar interspaces, and 54 from lumbosacral spaces.

As noted above, multiple disc lesions were found in 20 of the 96 positive operations. In most of these 20 cases, one disc was more diseased than the other. The major offending disc, or the only offending or pathologic disc, was located in the third lumbar space in 5 instances, at the fourth lumbar space in 46 cases, and at the lumbosacral level in the remaining 45 cases.

Although in no case in this group did the myelogram fail to give evidence of an extruded or protruded disc, there were cases in which the myelogram was misleading. Included in the latter were 28 cases termed major discrepancies and 12 termed minor discrepancies. A major discrepancy was considered present when a pathologic disc was found at operation with no indication of its presence by myelography or when a defect on the myelogram was unexplained by an abnormal disc at that level. Major discrepancies were present at 32 discs in 28 patients. Of these 32 discs involved, there were 25 false negative myelograms (pathologic disc but a negative myelogram at that level) and 7 false positive myelograms (positive myelogram but a normal disc at that level). Small defects in the myelogram in which large disc ruptures are found are not termed discrepancies, since the size of the defect is not necessarily in direct proportion to the size of the rupture.

The following disc lesions were accompanied by negative myelograms at that level: 1 bulging disc at the third interspace lumbar, 1 soft disc and 11 bulging discs at the fourth lumbar interspace, 2 soft discs, 7 bulging discs, and

3 scarred inspissated discs all at the lumbosacral space. In the following 7 cases positive myelograms were not explained by operative findings at that space; 2 at the third lumbar interspace, 2 at the fourth lumbar interspace, and 3 at the lumbosacral space. These figures are different from our previous findings that discrepancies are more common at the lumbosacral space than at the fourth space, since in this series discrepancies are about equal at the two spaces.

Four of the 28 cases had a false negative myelogram at one space and a false positive myelogram at another level. This explains the involvement of 32 spaces in the 28 major discrepancies.

There were 12 instances of minor discrepancies. In 7 cases the myelogram indicated a midline disc rupture but the operator designated the rupture as lateral. In 5 cases the myelogram indicated a lateral lesion and a midline rupture was found. These were not serious errors and would not result in missing a pathologic disc at operation or in preventing surgery when it was indicated.

The myelogram was completely accurate in the 60 remaining cases. Fifty-seven of these were positive and borne out by operative findings. Three negative myelograms were confirmed by operation.

This group of 100 persons who had clinical examination and myelography followed by surgery included some whose diagnosis was not certain before myelography. In reviewing these cases it was noted that the original clinical diagnosis before myelography was accurate, not only as to the diagnosis of a ruptured disc, but also in designating the proper level and site of the rupture in 57 of the 100 cases.

It is interesting to note that in only one of these 100 cases was the disc operation followed by spinal fusion. In this one case fusion was carried out because of an accompanying spondylolisthesis.

SUMMARY

One hundred consecutive cases have been analyzed in which hospital work-up, including myelogram, has been carried out prior to disc operation. Negative operative findings were present in 4 patients.

Over-all accuracy of the lumbar myelogram was found to be only 60 per cent. In 12 cases there were relatively unimportant discrepancies, but in 28 cases major discrepancies were found. This confirms our previous impression that a negative myelogram should not contraindicate the performance of disc surgery when symptoms and physical findings indicate operation. Nor is it necessary to subject the patient to myelography when the history, clinical course, and physical findings definitely indicate a disc lesion and the surgeon is able to determine the approximate location of the abnormal disc.

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CLINICAL STUDIES ON EFFECT OF BARIUM IN THE PERITONEAL CAVITY FOLLOWING RUPTURE OF THE COLON

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IN THE past year, we had an opportunity to study at firsthand the course of a patient who sustained a rupture of the colon with extravasation of barium into the peritoneal cavity following an opaque enema. At that time it became surprisingly evident that the literature contained few references to this subject. The obvious medicolegal implications of such reports undoubtedly deterred many authors, as did an understandable general reluctance to publicize mishaps of this nature. This is an unfortunate circumstance in view of the rather universal employment of barium sulfate as a contrast medium for opaque enemas.

Since the possibility of colonic rupture with barium extravasation is always present among those doing colonic studies, it was felt that a clinical evaluation of the course of such cases might be rewarding. It was hoped that criteria might thereby be established to aid in therapy and prognostication.

It was quite apparent that no single individual or group could (fortunately) accumulate sufficient personal experience to report an adequate study. In lieu of this we set out to compile the composite experiences of many radiologic centers. In order to accumulate sufficient material, questionnaires were sent to approximately 100 teaching institutions throughout the country. The inherent faults in such an approach were obvious. One of the greatest of these was the reluctance on the part of the investigators to impose too heavily on the generosity of their colleagues. To facilitate adequate response a compromise in the form of brevity had to be made. Nonetheless, it was felt that enough suitable data would be obtained to warrant evaluation.

The response was most gratifying, over eighty replies being received. Fifty of the institutions reported that they had never had patients who experienced a rupture of the colon in the course of a barium enema. This included some of the larger radiologic centers and encompassed a time period extending over many years. This again emphasized the relative rarity of the condition. Thirty-four of the institutions stated that they had at some time had patients with such an experience. Several of these reported more than one case, bringing the total of cases received up to fifty. These, plus three obtained from the teaching services of the University of Minnesota, made a total of fifty-three cases available for analysis.

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Only those cases which appeared to be genuine ruptures of the colon with free extravasation of barium into the peritoneal cavity were included. Cases in which barium was noted to have escaped into a fistulous tract or an abscess cavity, as well as cases in which air or fecal material alone extravasated, were excluded. Excluded, also, were those cases in which the rupture was retroperitoneal.

The suspected diagnosis prior to barium enema in the reported cases encompassed nearly all the indications for performing such an examination. Among these, three categories predominated: suspected carcinoma of the colon (13 cases), re-evaluation of the colon through a colostomy opening (12 cases), and suspected colonic obstruction (8 cases). In most institutions, suspected carcinoma ranks high on the list of indications for a barium enema. It is not surprising to find colonic obstruction as a leading pre-enema diagnosis in these cases. What is surprising, however, is the relatively high incidence of perforation in the presence of a colostomy.

In five of the colostomy cases an abnormality of the bowel wall was found to be present. In each case this was related to the original pathology. In three other cases, perforation was in all probability related to a weakening of the colon near the colostomy site as a result of herniation of the bowel at this point. Two cases showed tears in the bowel wall at the site of an inflatable balloon. Of the remaining two colostomy cases, one was a direct perforation of the bowel by catheter insertion and the other was of undetermined etiology.

It might be appropriate here to mention the fact that several other instances of colonic rupture were attributed to the direct trauma of an inflatable balloon. In one case, rupture of the balloon immediately preceded the colonic rupture. It has been brought to our attention by proctologists that rectal laceration has been noted following the use of an inflatable balloon. This does not obviate the fact that inflatable balloons are an extremely valuable adjunct to the proper examination of the colon in many instances, and it should be borne in mind that abrasions of the anterior rectal wall have been noted not uncommonly at sigmoidoscopy following an ordinary cleansing enema.[15]

The etiologies of the colonic perforations are tabulated in Table I.

In 35 of the 49 cases where the information is available, the rupture of the colon occurred during the course of the barium enema. Seven other cases were thought to have ruptured immediately following the barium enema, and one case twenty-four hours later. As mentioned previously, four were ruptured prior to the barium study of the colon.

There appears to have been no unanimity of opinion regarding the therapeutic procedures to be undertaken in the event of rupture. Thus, 32 of the 53 cases were handled by laparotomy, while 21 were treated by conservative measures. In evaluating these cases, it must be remembered that some occurred prior to the antibiotic era, and thus the details of both medical and surgical therapy will vary from case to case.

The immediate results of the two methods of therapy have been set down in Table II. The over-all mortality rate among those treated surgically was 47 per cent as opposed to an over-all mortality rate of 58 per cent in the group

TABLE I. ETIOLOGY OF COLONIC PERFORATION (AS REPORTED)

Trauma	
By enema tip or balloon	10
By proctoscopy	4
By fractured rib	1
Carcinoma of the colon	10
Diverticulitis	5
Congenital anomalies of the colonic wall	4
Ulcerative colitis	2
Lymphopathic venereum with stricture	2
Chronic herniation of colostomy	2
Breakdown of colostomy stoma	1
Inflammatory lesion of colonic wall	1
Diverticulosis	1
Volvulus (?) of the colon	1
Appendical abscess	1
Mesenteric thrombosis	1
Pelvic inflammatory disease	1
Adhesions	1
Not stated	5

treated by conservative measures. Among those in the surgical group, approximately 53 per cent were listed as being in good or fair condition immediately following the rupture, while approximately 47 per cent were listed as poor or moribund immediately following the rupture. These figures were almost identically reversed in the group treated conservatively, a slightly higher percentage of patients being in the poor or moribund category as opposed to the good or fair grouping. This factor might have influenced the slight difference in over-all mortality rates between the medical and surgical groups.

TABLE II. IMMEDIATE MORTALITY

TREATMENT	TIME*	DIED	LIVED
A. Surgical			
	Less than 3 hours	6	4
	4 to 6 hours	3	6
	7 to 12 hours	1	3
	13 to 24 hours	3	1
	25 to 72 hours	3	
	More than 72 hours	1	
	Not stated		1
Total		17 (53%)	15 (47%)
B. Medical (conservative)		8 (42%)	11 (58%)
Total†		25 (49%)	26 (51%)

*Time elapsing between rupture and institution of surgical treatment.
†Fate of two cases treated conservatively not stated.

The breakdown of surgical mortality rates, in respect to the time elapsing between the colonic rupture and the institution of surgical treatment, may also be seen in Table II. It is noted that within the first three hours the mortality rate was considerably lower than in the next nine-hour period. From this point on, there was again a sharp drop in the mortality rate. This latter drop was due in part to the fact that the majority of patients operated upon in the first twelve-hour period were classed predominantly as poor or moribund prior to surgery, while those operated upon in the next twelve-hour period were classified chiefly as good or fair in the preoperative period.

From the combined surgical and medical mortality figures, it may be deduced that the patient has approximately a 50 per cent chance of surviving the immediate postrupture period and probably a slightly better chance if treated by laparotomy within a three-hour period.

Fig. 1 (Case 1, U.M.H. No. 783101).—Roentgenogram made several hours after perforation showing free air and barium in the peritoneal cavity.

Follow-up reports were available in twenty-three of the twenty-five surviving cases. The period of observation ranged from two months to five years and averaged approximately eighteen months.* Of these cases, seven (30 per cent) developed adhesions, necessitating repeated surgery. The percentage of cases developing adhesions did not appear significantly higher in the group treated conservatively than in the surgical group. Likewise, there appeared to be no significant correlation between the development of adhesions and the lapse of time between perforation and surgery.

CASE REPORTS

CASE 1 (U.M.H. No. 783101).—A 75-year-old white woman came to the outpatient department complaining of abdominal pain, anorexia, and weight loss. A barium enema was done on Oct. 16, 1947, using an inflatable balloon catheter for purposes of retention.

*One case, treated conservatively, survived for sixteen years without evidence of complications, but was not included in computing the average follow-up period.

Examination at the time was felt to be negative. The patient returned to her home, but was awakened at 5:30 A.M. the following day by the sudden onset of abdominal pain, centered chiefly in the left lower quadrant. Associated with the pain were nausea, vomiting, and the passage of bright red blood by rectum. Positive findings on readmission were a distended, quiet, and rigid abdomen associated with a moderate elevation of temperature.

Roentgen examination at this time revealed free air and barium in the peritoneal cavity (Fig. 1). The patient was operated upon eight hours after the presumed time of perforation. A carcinoma of the sigmoid with perforation proximal to it was found at surgery, and free barium was present in the sigmoid mesentery and in the left lower quadrant. The patient died of peritonitis eight and one-half hours postoperatively.

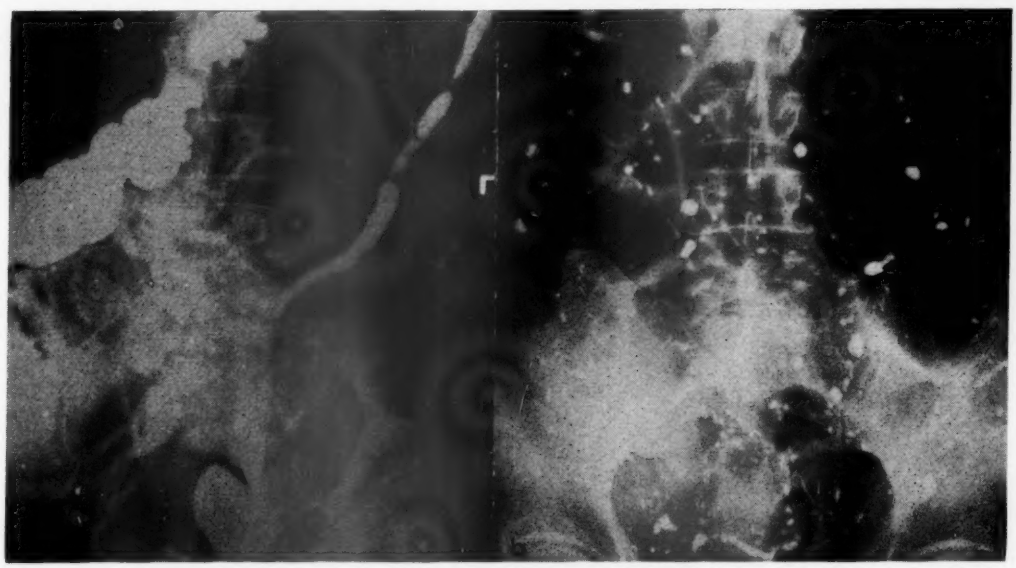

Fig. 2 (Case 2, U.M.H. No. 739772).—*a*, Roentgenogram after evacuation of barium enema shows free barium in the peritoneal cavity. *b*, Roentgenogram four years after perforation shows residual barium nodules and evidence of partial small bowel obstruction.

CASE 2 (U.M.H. No. 739772).—A 66-year-old white man had had a resection of two carcinomas of the descending colon with establishment of a colostomy in the three years prior to admission. He complained on admission of abdominal pain, cramps, and diarrhea of two weeks' duration. At 10:00 A.M. on Dec. 31, 1943, a barium enema was administered through the colostomy orifice employing a balloon catheter. In the course of the examination the patient deveolped acute abdominal pain, tachycardia, and signs of peritoneal irritation. Free barium was noted in the peritoneal cavity (Fig. 2,*a*). The procedure had been carried out at another hospital. The patient was then transferred to the University of Minnesota Hospitals where surgery was carried out within fourteen hours. Two perforations of the colon were found near the site of the colostomy. The peritoneal cavity, which was full of feces, barium, and blood, was irrigated with saline, and sulfanilamide and sulfathiazole were instilled. A transverse colostomy and an enterostomy were established. In spite of a stormy postoperative course, the patient recovered and was discharged.

He was readmitted on April 24, 1944. An adenocarcinoma of the ileocecal valve was excised, and an ileosigmoidoscopy established.

Upon third admission, April 2, 1945, a right perinephric abscess, the result of a foreign body (barium) reaction, was drained.

On his fourth admission, Oct. 27, 1947, the patient showed signs of intermittent small bowel obstruction. At surgery, multiple adhesions were found related to barium depositions (Fig. 2,*b*). In the mid-small bowel, there were several areas of narrowing apparently related to fibrous reaction about barium particles within the serosa. Numerous lymph nodes were

found to contain barium. An enterolysis was carried out and the postoperative course was complicated by pneumonia, following which the patient rapidly lost ground and died on the fifth postoperative day.

CASE 3 (M.V.A.H. No. 114-115).—A 63-year-old white farmer with a history of numerous rectal fistulas was treated in 1933 by a sigmoid colostomy. During the subsequent years the patient developed increasing prolapse of the colostomy. He was admitted in May, 1951, for repair of the colostomy and also an inguinal hernia.

On physical examination the bowel was found to prolapse as much as five inches onto the anterior abdominal wall. No ulcerations of the bowel could be found. Laboratory data were within normal limits.

Fig. 3 (Case 3, M.V.A.H. No. 114115).—*a*, Roentgenogram made the day after perforation shows barium free in the peritoneal cavity, and lining bowel wall. *b*, Roentgenogram the day after operation shows partial removal of the free barium. Compare with *a*.

On May 11, 1951, a barium enema was instilled through the colostomy opening into the proximal colon. The colon was filled and no definite evidence of intrinsic abnormality found. On completion of the examination the patient complained of pain and was unable to evacuate the enema. An x-ray examination of the abdomen at this time showed free barium in the peritoneal cavity and along the bowel walls (Fig. 3,*a*).

On May 14, 1951, the patient was explored. Throughout the abdominal cavity, thick, white, sticky barium was found in large quantities. No definite perforation was located. A cecostomy was performed and the patient recovered satisfactorily (Fig. 3,*b*). The cecostomy was closed in September, 1951, and the original colostomy revised. The patient has been discharged from the hospital with no apparent discomfort or difficulties in the ten months he has been under observation.

EXPERIMENTAL DATA

It has been shown that the peritoneal cavity reacts to barium sulfate in much the same fashion as to any inert foreign substance.[8, 10, 19] Thomas,[19] in

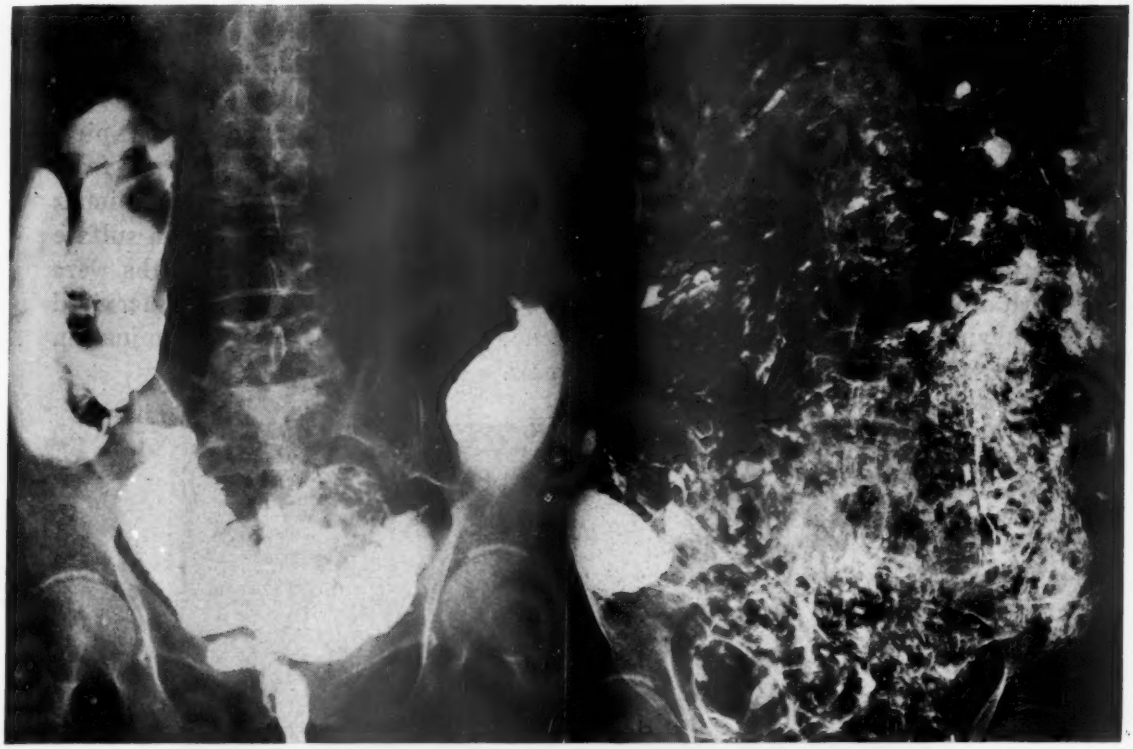

Fig. 4.—Rectum perforated during barium enema which was preceded by proctoscopic biopsy of a mass pressing on bowel wall. *a*, Extravasation of barium into peritoneal cavity (film reversed). *b*, Film made eight days later showing barium widely dispersed. The patient was free of complications ten months later. (Films by courtesy of Mallinckrodt Institute of Radiology.)

Fig. 5.—Roentgenogram showing perforation of lower colon with extravasation of barium. (Film by courtesy of contributing radiologist.)

1936, reported his experimental results on the disposal of barium sulfate in the peritoneal cavity. His findings are similar to those recorded in our experimental data.

Our studies were carried out on thirty-one medium-sized guinea pigs. Barium sulfate was injected singly and in combination with a guinea pig fecal suspension into the peritoneal cavity. In addition, in one group of animals the lower colon was perforated, using a No. 15 gauge needle, and barium sulfate instilled via the perforation. In a sixty-day follow-up period, no deaths were attributable to the intraperitoneal barium sulfate. Animals were sacrificed at varying intervals to study the histopathologic responses. X-ray examination was carried out periodically on all animals.

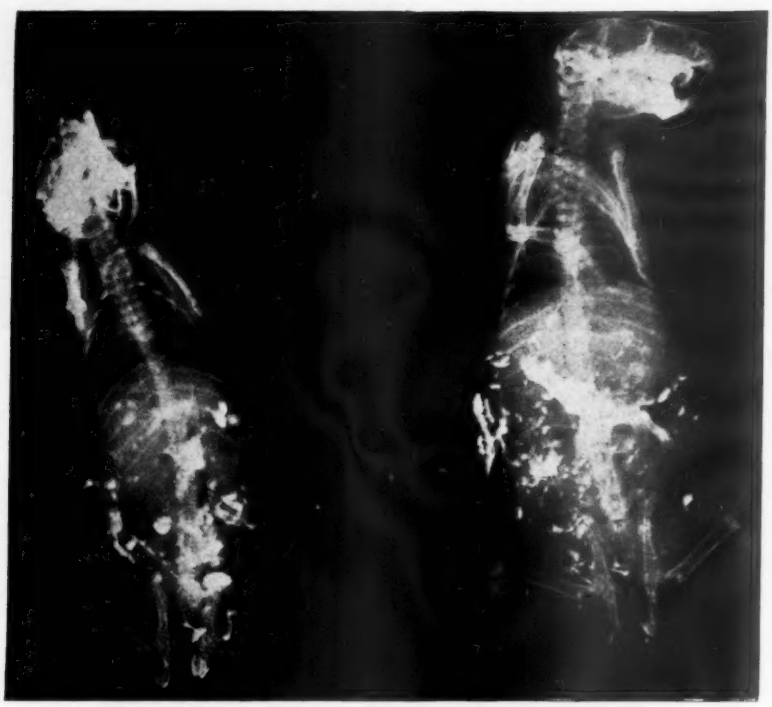

Fig. 6.—Guinea pigs. Appearance of barium twenty-six days after the injection of 10 c.c. of a 50 per cent barium sulfate mixture into the peritoneal cavity.

Immediately following injection of 10 c.c. of a 50 per cent barium sulfate mixture, the barium was found to be widely distributed throughout the peritoneal cavity (Fig. 6). Within thirty minutes the barium was found to be accumulating in the omentum and on the walls of the viscera. With irrigation the barium could be moderately well dislodged, except for a few tenacious particles. Studies at 60 minutes throughout 120 minutes showed a progressive tendency for the barium to be collected by the omentum, becoming more adherent. When large amounts (15 c.c. of the mixture) were injected, it was noted that the barium had accumulated in large omental pseudocysts (Fig. 7,*a* and *b*).

Microscopic examination was carried out in all these instances with the following results. At 5 minutes after introduction of barium into the peri-

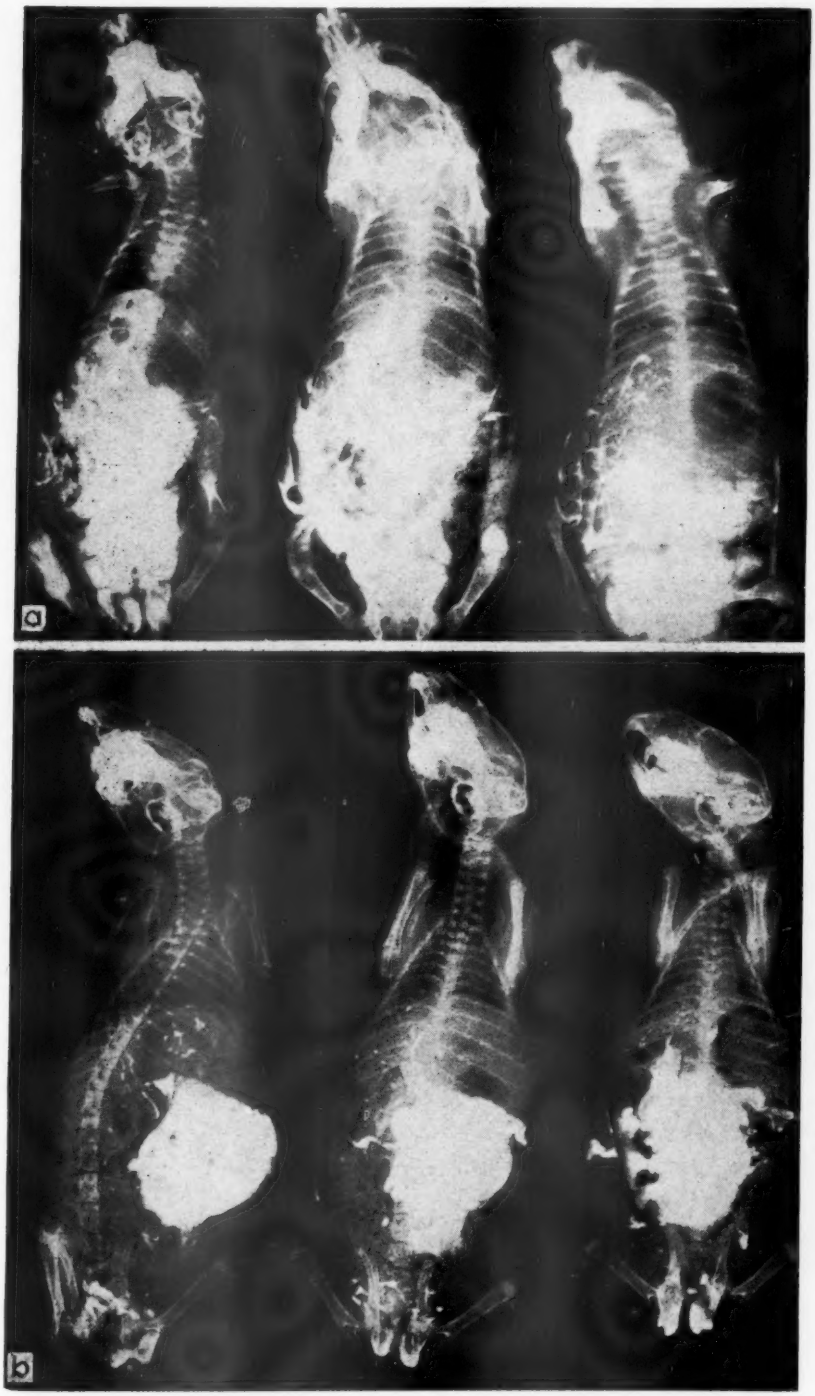

Fig. 7.—Guniea pigs. Appearance following intraperitoneal injection of 15 c.c. of 50 per cent mixture of barium sulfate. *a*, Immediately after the injection. *b*, Six days later showing the omental cyst formation.

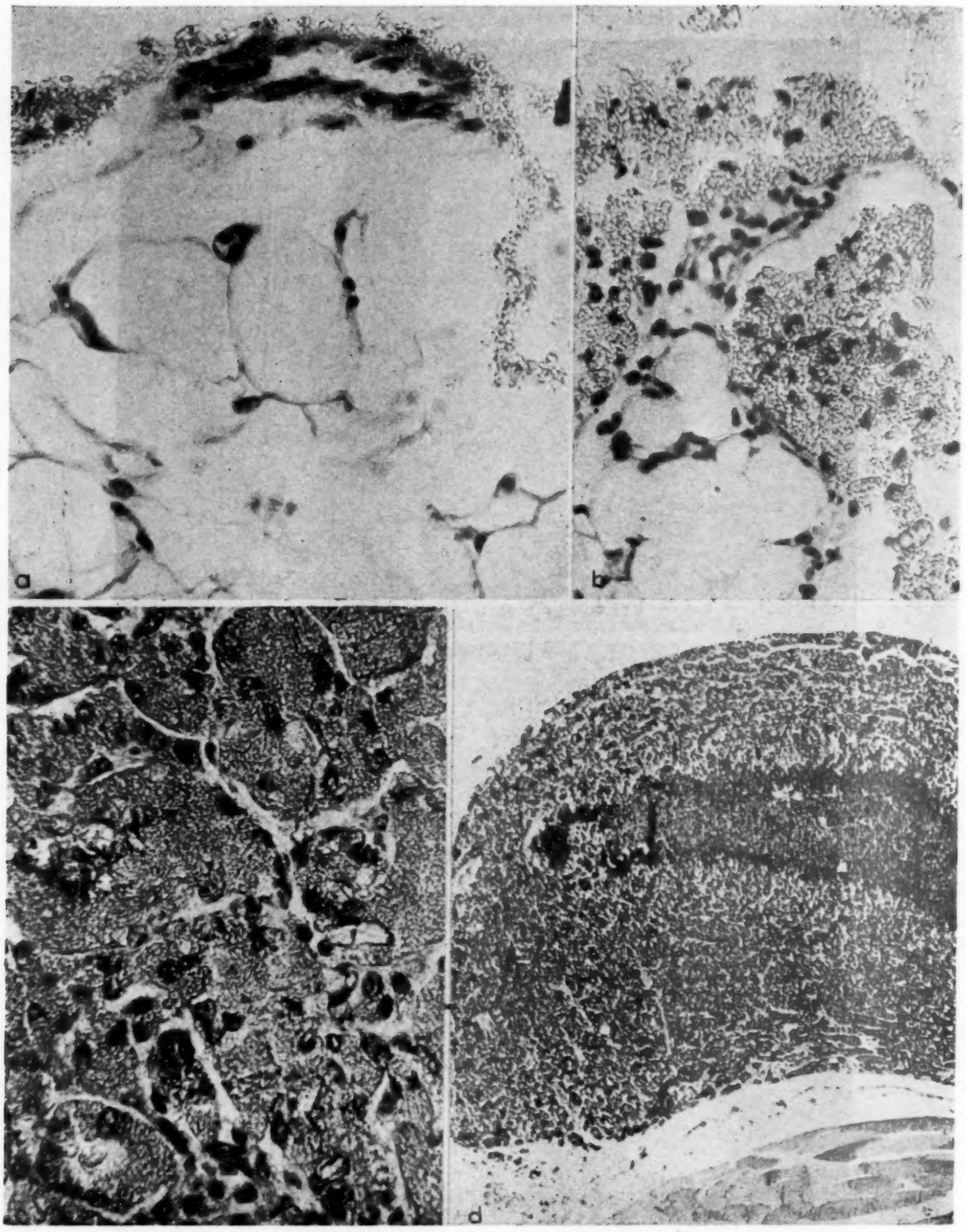

Fig. 8.—Microscopic sections from guinea pigs after experimental introduction of barium into peritoneal cavity.

a, Omentum five minutes after introduction of barium into peritoneal cavity. Note the complete absence of tissue reaction; the barium may be seen as a thin layer of refractile crystals on the serosal surfaces.

b, Omentum 120 minutes after introduction of barium into peritoneal cavity; perivascular inflammatory exudate is present with migration of inflammatory cells into barium.

c, High-power view of phagocytized barium showing giant cells and the typical macrophages.

d, Relatively large mass of barium adherent to peritoneum of anterior abdominal wall twen'y-six days after introduction of barium into peritoneal cavity. The central area is unorganized mass of barium surrounded by large masses of phagocytes.

toneal cavity of a guinea pig, a very thin layer of barium particles adhered to the serosal surfaces; there was no evidence of fibrin formation, inflammation, or other reaction on the part of the tissues (Fig. 8,*a*). At 30 minutes, thicker strands of barium were found on the serosal surfaces but at this time no morphologic manifestations of tissue reaction were apparent. At 60 minutes, however, perivascular inflammatory cells had appeared and a few of these cells were beginning to migrate into the adherent masses of barium. After 90 minutes, this process had become much more severe and was reflected by margination of leukocytes in the small blood vessels, the invasion of the adherent barium by these inflammatory cells becoming more marked. After 120 minutes, these changes were very extensive, the adherent barium particles were heavily infiltrated by inflammatory cells, and perivascular inflammatory infiltration was very prominent (Fig. 8,*b*). Thus, a reaction on the part of the tissue to the presence of barium was apparent as early as 60 minutes following introduction of the barium into the peritoneal cavity, and this reaction progressed very rapidly so that at two hours the barium masses were heavily infiltrated by inflammatory cells.

The fate of these barium masses was perfectly apparent in the sections studied twenty-six days after introduction; the barium was present in small nodular aggregates on the serosal surface of the anterior abdominal wall, peritoneum, intestine, and other visceral organs. The smaller masses were composed almost entirely of phagocytic cells and foreign body giant cells; the former were rather large irregular, circular, or ovoid cells consisting primarily of cytoplasm which was filled with small refractile granules of barium; one or more small nuclei had usually been crowded to the periphery of these cells (Fig. 8,*c*). Dense fibroblastic proliferation with some vascularization was present on the periphery of such nodules. In several areas (particularly on the serosal aspect of the bowel) this fibroblastic process of organization had formed firm, fibrous adhesions to adjacent or contiguous organs. Larger masses of barium had a similar composition with the exception that the central areas of such masses consisted only of barium particles without the presence of phagocytic cells, the latter being found in the periphery of such masses and being surrounded, in turn, by a fibroblastic wall. Still more excessive quantities of barium (Fig. 8,*d*) were localized in a similar manner with the exception that not only did the central area contain unorganized barium but large quantities of serum as well. The wall of such a cystic cavity has otherwise a composition identical with the other masses previously described. Thus the fate of free barium in the peritoneal cavity is a process of successive aggregation, partial or complete phagocytosis (dependent upon total quantity), and fibroblastic encapsulation with extensive adhesion formation. Larger masses are similarly walled off with the addition of central cyst formation.

DISCUSSION

The problem of barium sulfate in the peritoneal cavity following a rupture in the upper gastrointestinal tract has been dealt with to some extent.[2, 6, 8, 11-13, 17, 18] Gross,[6] in 1941, reported two cases of perforated peptic

ulcer with extravasation of barium into the peritoneal cavity. He collected twenty-five additional cases from the literature and came to the conclusion that the morbidity rate bore a direct relation to the amount of barium found in the peritoneal cavity. It was also his opinion that because of early exudation in these cases, immediate exploration with removal of as much barium as possible should be done. If this were not feasible, the omentum which contained the barium should be excised.

Paas,[13] doing experimental work on dogs, came to the conclusion that the survival rate depended on the amount of barium used and the time factors involved. In large dogs, 70 to 140 c.c. of barium caused death in three days.

Bergh and Borman,[2] in a yet unpublished work, showed that 10 to 30 c.c. of sterile barium sulfate did not cause death in dogs when injected directly into the peritoneal cavity. In contradistinction, barium which was contaminated by passage through the esophagus into the stomach and then through a perforation into the peritoneal cavity caused death in all dogs.

Reports from the literature regarding perforation of the lower colon by instrumentation, by insertion of enema tip, and by spontaneous occurrences in certain disease states, indicate that a mortality rate ranging from 40 to 100 per cent may be expected.[1, 3-5, 9, 11, 14-16] Most series averaged approximately a 50 per cent mortality rate and most authors noted that the mortality rate rose with delayed surgical intervention.

Recently Greene and Greene[5] reported an instance of traumatic perforation of the colon in a patient with a colostomy in the course of irrigation with a catheter. These authors state that a review of the literature for the past eighteen years indicates only one report of a similar complication. This is somewhat surprising to us in view of the relatively high incidence of such an occurrence in our series.

There appears to be little justification in attempting to correlate the morbidity and mortality rates encountered in animal work with those expected in clinical cases. Histological studies, however, appear to coincide with the changes found in the cases studied here.

From our data and from the work of others it has been shown that barium sulfate incites a rather severe peritoneal reaction. There appears to be a short period of grace, extending perhaps up to two hours, during which period surgical intervention appears to have produced optimal results. Since it appears practically impossible to remove all of the barium, even in those cases with immediate surgical intervention, adhesions are to be expected in every instance, although not all of these will be clinically significant.

SUMMARY

1. Reports from questionnaires sent to over 100 radiological centers indicate that perforation of the colon with extravasation of barium sulfate into the peritoneal cavity is a rare occurrence.

2. Fifty-three cases are reviewed in this report.

3. There is a relatively high percentage of perforation in enemas (a) performed via colostomy stoma, (b) utilizing an inflatable balloon, and (c) immediately following proctoscopic examination.

4. The over-all mortality rate was 51 per cent.

5. The operative survival appears to be greater if the surgery can be carried out within three hours of the perforation. Survival rate in the next nine hours shows a considerable drop.

6. From clinical and histologic studies it appears that immediate surgery is necessary to remove any substantial amount of extravasated barium sulfate.

7. Clinically significant adhesions developed in 30 per cent of 23 cases followed for an average of 18 months.

8. Adhesions were as frequent in those cases where an attempt was made to remove the barium sulfate as in those cases treated conservatively.

9. Data obtained from guinea pig studies indicated the cellular response to be expected when free barium sulfate was present in the peritoneal cavity.

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ADDENDUM

One of the cases reported here has been published separately in Ann. Surg. **135**: 564, 1952.

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SULFADIMETINE, A NEW SULFONAMIDE FOR THE TREATMENT OF URINARY INFECTIONS*

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THIS report deals with the therapeutic effects of sulfadimetine† (6-sulfanilamido-2, 4-dimethylpyrimidine) in forty patients with urinary tract infections due, in most cases, to gram-negative bacilli. The claims for this drug are that: (1) It is the least acetylated of the sulfapyrimidine derivatives, (2) it is very soluble in the unconjugated state in urine within a range of pH 5.5 to 8, (3) it is free of toxicity, and (4) it has high therapeutic potency in experimental animals.[1, 2]

COMPARATIVE IN VITRO ACTIVITY OF SULFADIMETINE AND OTHER SULFONAMIDES

The comparative in vitro sensitivity of 88 strains of various bacterial species to 4 sulfonamides was determined by a standardized serial tube dilution method.[3, 4] With this method the bactericidal titer was taken to be the lowest concentration required to prevent macroscopically visible growth in 24 hour cultures (at 37° C.) which on subculture for 48 hours did not reveal any growth. From previous studies it was possible to state that a strain could be considered sensitive, that is to say, clinically eradicable, by the usual therapeutic doses of sulfonamides, if the bactericidal titer in vitro by this method was 250 mg. per cent or less, and resistant if 500 mg. per cent or more. Except for Salmonella and Shigella, all the strains tested were freshly isolated from infected urines.

Table I demonstrates not only the familiar fact that different strains of a given bacterial species vary widely in their sensitivity to the same and to various sulfonamides, but that sulfadimetine has some advantage over other sulfonamides in use. Table II provides detailed data on the range of sensitivity of various strains within a species. Sulfadimetine and Sulfamethazine‡ were clearly superior to sulfadiazine and sulfacetimide in most instances.

CLINICAL OBSERVATIONS

Forty unselected patients with acute and chronic urinary tract infections were given sulfadimetine. The detailed data are listed in Table III. All patients had pyuria, positive urine cultures, and the usual clinical signs and

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†Commercially known as Elkosin. Manufactured by Ciba Pharmaceutical Products, Inc., Summit, N. J.

‡2-sulfanilamido-4, 6-dimethypyrimidine, an isomer of sulfadimetine.

TABLE I. COMPARATIVE IN VITRO SENSITIVITY OF BACTERIA TO SULFADIMETINE, SULFAMETHAZINE, SULFADIAZINE, AND SULFAFACETIMIDE

SPECIES	TOTAL NUMBER OF STRAINS	SENSITIVITY TO SULFADIMETINE AS COMPARED TO OTHER SULFONAMIDES			RESISTANT TO ALL 4 SULFONAMIDES
		MORE SENSITIVE	EQUALLY SENSITIVE	LESS SENSITIVE	
		NUMBER OF STRAINS	NUMBER OF STRAINS	NUMBER OF STRAINS	NUMBER OF STRAINS
Esch. coli.	11	4	3	1	3
A. aerogenes	8	4	0	1	3
Ps. aeruginosa	20	2	3	4	11
β proteus vulgaris	15	1	0	3	11
Staph. aureus	15	3	2	2	8
B. hemolytic Streptococci	6	3	2	0	1
Salmonella	9	5	4	0	0
Shigella	4	0	4	0	0
Total	88	22	18	11	37

symptoms. Twenty-four had calculi, stricture, prostatic obstruction, or were on constant catheter drainage. Obstructive lesions, if present, were treated during sulfadimetine therapy. Twenty-nine patients had failed to respond to prior treatment with other antibiotics: penicillin (12), penicillin and Aureomycin (10), Aureomycin alone (4), penicillin, Chloromycetin and Aureomycin (1), penicillin and Sulfamethazine (1), and Chloromycetin (1).

The urine specimens for culture were obtained by catheterization in all women and in most men. In a few instances a clear-voided specimen was obtained in male patients. Cultures were taken at intervals of 1 to 3 days and

TABLE II. COMPARATIVE IN VITRO SENSITIVITY OF SEVERAL STRAINS OF A GIVEN SPECIES OF BACTERIA TO FOUR SULFONAMIDES (SIZE OF INOCULUM 2,000 TO 8,000 BACTERIA)

STRAIN	BACTERICIDAL TITER IN MG. % OF DRUG IN NUTRIENT BROTH				NUMBER OF STRAINS WITHIN EACH TYPE OF SENSITIVITY
	SULFADIMETINE	SULFAMETHAZINE	SULFACETIMIDE	SULFADIAZINE	
Esch. coli I	50	100	250	1,000	4
Esch. coli II	50	50	500	1,000	3
Esch. coli III	500	250	500	1,000	1
Esch. coli IV	750	750	750	1,000	3
A. aerogenes I	250	500	500	1,000	4
A. aerogenes II	500	100	500	1,000	1
A. aerogenes III	750	750	750	750	3
Ps. aeruginosa I	250	1,000	1,000	1,000	2
Ps. aeruginosa II	250	250	500	1,000	3
Ps. aeruginosa III	750	250	750	1,000	4
Ps. aeruginosa IV	1,000	1,000	1,000	1,000	11
B. proteus vulgaris I	250	1,000	1,000	1,000	1
B. proteus vulgaris II	750	500	1,000	1,000	3
B. proteus vulgaris III	750	750	1,000	1,000	11
Staph. aureus I	250	500	500	500	3
Staph. aureus II	250	250	500	1,000	2
Staph. aureus III	250	100	750	500	2
Staph. aureus IV	1,000	1,000	1,000	1,000	8
β hemolytic streptococcus I	100	250	250	500	3
β hemolytic streptococcus II	50	50	250	250	2
β hemolytic streptococcus III	750	750	750	1,000	1
Salmonella I	250	750	750	750	5
Salmonella II	500	500	750	1,000	4
Shigella I	100	100	250	500	4

TABLE III. THE DATA OF FORTY PATIENTS WITH URINARY INFECTIONS TREATED WITH SULFADIMETINE

CASE NUMBER	PRIMARY DIAGNOSIS	URINE CULTURES BEFORE SULFADIMETINE	IN VITRO SENSITIVITY TO SULFADIMETINE BACTERICIDAL TITER MG. %	URINE CULTURES AFTER SULFADIMETINE	CHEMOTHERAPY PRIOR TO SULFADIMETINE	SULFADIMETINE DOSAGE (GM. PER DAY)	SULFADIMETINE DAYS	SULFADIMETINE BLOOD LEVEL MG. %	FOLLOW-UP AFTER TREATMENT (DAYS)	FINAL RESPONSE
1	Cystitis, postoperative	*Esch. coli*	100	Sterile	None	4	4	4.0 to 16.8	55	Cured
2	Cystitis, postoperative	*Esch. coli*	-	Sterile	Penicillin Aureomycin	4	8	8.6	23	Cured
3	Cystitis, postoperative	*Esch coli*	-	Sterile	Aureomycin	4	4	7.6	20	Cured
4	Cystitis, postoperative	*Esch. coli*	-	Sterile	Penicillin	6	12	10.4	52	Cured
5	Cystitis, postoperative	*B. paracolon*	250	Sterile	Penicillin Aureomycin	4	5	-	116	Cured
6	Cystitis, postoperative	*B. proteus*	250	Sterile	Penicillin Aureomycin	4	4	-	213	Cured
7	Cystitis, postoperative	*B. proteus*	1,000	*B. proteus*	Penicillin Aureomycin Chloromycetin	4	4	-	-	Failure
8	Cystitis, postoperative	*B. proteus*	750	*B. proteus*	Penicillin	5	9	-	-	Failure
9	Cystitis, postoperative	*A. aerogenes*	-	Sterile	Penicillin	4	5	-	42	Cured
10	Cystitis, postoperative	*A. aerogenes*	250	*Ps. aeruginosa*	Aureomycin	4	4	-	-	Failure
11	Acute cystitis	*Esch. coli*	-	Sterile	None	4	2	-	15	Cured
12	Chronic cystitis	*Esch. coli*	250	Sterile	Penicillin Aureomycin	4	6	-	35	Cured
13	Chronic cystitis Carcinoma bladder	*Ps. aeruginosa*	-	*Ps. aeruginosa* *B. proteus*	Penicillin	4	14	-	-	Failure
14	Cystitis following prostatectomy	*Esch. coli*	750	*Esch. coli* *Ps. aeruginosa*	None	4	11	5.7 to 7.3	-	Failure
15	Cystitis following prostatectomy	*Esch. coli*	500	*Esch. coli* *Staph. aureus* *Ps. aeruginosa*	None	4	5	7.6 to 8.1	-	Failure
16	Acute postoperative cystitis and pyelonephritis	*Esch. coli*	-	Sterile	Penicillin Sulfamethazine	4	3	-	30	Cured
17	Acute pyelonephritis	*Esch. coli*	250	Sterile	None	4	5	-	110	Cured

18	Acute pyelonephritis	*Esch. coli*	100	Sterile	None	4	6	7.1 to 7.3	14	Cured
19	Pyelonephritis during pregnancy	*Esch. coli*	100	Sterile	Penicillin	4	4	-	30	Cured
20	Acute pyelonephritis and cystitis due to renal calculi	*B. proteus*	250	Sterile	Chloromycetin	4	3	2.1	20	Cured
21	Cystitis, postoperative	*Esch. coli* *Staph. albus*	250 500	Sterile	Penicillin	4 3	6 3	8.4	28	Cured
22	Cystitis, postoperative	*B. proteus* *Ps. aeruginosa*	250 250	Sterile	Penicillin Aureomycin	4	3	6.2 to 11.2	29	Cured
23	Cystitis, postoperative	*B. proteus* *Ps. aeruginosa* (heavy growth)	750 >1,000	*B. proteus* *Ps. aeruginosa* (6 to 8 colonies)	Penicillin Aureomycin	4	5	3.9	91	Good
24	Cystitis, postoperative	*B. proteus* *Ps. aeruginosa*	-	*E. coli*	Penicillin Aureomycin	3 to 4	17	-	-	Failure
25	Cystitis, postoperative	*B. paracolon* *B. proteus*	-	*B. proteus* *Ps. aeruginosa*	Penicillin Aureomycin	4	8	-	-	Failure
26	Acute cystitis	*Esch. coli* *B. proteus*	100 250	Sterile	None	4	4	5.3	88	Cured
27	Chronic cystitis	*B. proteus* *Ps. aeruginosa*	250 250	Sterile	Penicillin Aureomycin	4	-	-	42	Cured
28	Chronic cystitis Carcinoma bladder	*Esch. coli* *B. proteus* *Ps. aeruginosa*	-	Sterile	Aureomycin	4	17	6.0 to 11.0	30	Cured
29	Chronic cystitis Carcinoma bladder	*A. aerogenes* *Ps. aeruginosa* Nonhemolytic streptococci *Staph. albus*	250 1,000 500 100	*Ps. aeruginosa* Nonhemolytic Streptococci	Pencillin	4	5	-	-	Failure
30	Chronic cystitis Carcinoma bladder	*B. paracolon* *Ps. aeruginosa*	-	*Ps. aeruginosa*	None	4	20	7.4 to 10.6	-	Failure
31	Cystitis following prostatectomy	*Staph. albus hemolyticus* *Staph. albus nonhemolyticus* *Esch. coli* *Ps. aeruginosa*	100 250 100 250	Sterile	Penicillin	4	15	6.8 to 9.4	271	Cured
32	Cystitis following prostatectomy	*Staph. aureus hemolyticus* *Staph. albus hemolyticus* *Staph. aureus nonhemolyticus* *Esch. coli*	-	Sterile	Penicillin	4	8	3.3	25	Cured

TABLE III.—CONT'D

CASE NUMBER	PRIMARY DIAGNOSIS	URINE CULTURES BEFORE SULFADIMETINE	IN VITRO SENSITIVITY TO SULFADIMETINE BACTERICIDAL TITER MG. %	URINE CULTURES AFTER SULFADIMETINE	CHEMOTHERAPY PRIOR TO SULFADIMETINE	SULFADIMETINE DOSAGE (GM. PER DAY)	SULFADIMETINE DAYS	SULFADIMETINE BLOOD LEVEL MG. %	FOLLOW-UP AFTER TREATMENT (DAYS)	FINAL RESPONSE
33	Cystitis following prostatectomy	*Esch. coli* *Ps. aeruginosa* (heavy growth)	500 500	*Esch. coli* (3 colonies) *Ps. aeruginosa* (6 colonies)	Penicillin	4	21	7.8 to 8.8	12	Good
34	Cystitis following prostatectomy	*Esch. coli* *Ps. aeruginosa*	500 >1,000	*Esch. coli* *Ps. aeruginosa* *Staphylococcus aureus*	Penicillin	4	30	5.7 to 8.3	-	Failure
35	Cystitis following prostatectomy	*Ps. aeruginosa* *Streptococcus faecalis*	-	*Ps. aeruginosa*	Aureomycin	4	14	6.3	-	Failure
36	Cystitis following prostatectomy	*Esch. coli* *Ps. aeruginosa*	-	*Esch. coli* *Ps. aeruginosa* *B. proteus*	None	4	15	7.3 to 9.9	-	Failure
37	Cystitis secondary to urethral stricture	*A. aerogenes* *Ps. aeruginosa*	250 750	*Ps. aeruginosa*	Penicillin Aureomycin	4	11	8.8	52	Good
38	Acute pyelonephritis following cystoscopy	*Esch. coli* *Ps. aeruginosa*	-	Sterile	None	4	5	8.2	30	Cured
39	Acute pyelonephritis Chronic cystitis	*A. aerogenes* *Esch. coli*	250 100	Sterile	Penicillin	4	23	6.5	50	Cured
40	Acute pyelonephritis and cystitis due to renal calculi	*Staph. aureus* *Diphtheroids*	100	Sterile	None	4	7	10.9 to 11.5	42	Cured

were repeated about twice in a 7 to 15 day period after termination of treatment. Thereafter, follow-up was carried out for periods ranging from 12 to 271 days (Table III), except when sulfadimetine had proved ineffective.

Twenty of the infections were due to a single organism, and 20 were due to more than one. *Escherichia coli* was isolated in 22 patients, *Pseudomonas aeruginosa* in 15, *Bacillus proteus vulgaris* in 11, *Staphylcoccus aureus* or *albus* in 8, *Aerobacter aerogenes* in 5, paracolon bacilli in 3, Streptococci in 2, and diphtheroids in 1.

An initial oral dose of 2 Gm. of sulfadimetine by mouth was followed by 4 Gm. daily in divided doses. Alkali was not given and no attempt was made to maintain a minimum daily fluid intake. Most of the patients were treated for 4 to 8 days, or longer if bacilluria was still present. If improvement did not result in 15 days the drug was considered ineffective and was discontinued.

Sulfadimetine was rapidly absorbed from the gastrointestinal tract. Following a single oral dose of 2 Gm., maximum blood concentration of free sulfonamide (6 to 8 mg. per cent) was reached in 2 to 3 hours, and levels of 2 to 6 mg. per cent were maintained for 4 to 6 hours therafter.[5] Blood levels of 6 to 12 mg. per cent of free sulfonamide were easily maintained on 4 Gm. of the drug daily. Determinations of free and total sulfonamide in the blood and urine of patients receiving sulfadimetine revealed a low order of acetylation, 80 to 95 per cent of the total sulfonamide being in the free form.[5]

Toxic reactions were not observed. Renal damage did not occur in any patient. There was no rise in blood nonprotein nitrogen, no oliguria, crystalluria, or hematuria, and phenolsulfonphthalein excretion was normal. Gastrointestinal or allergic reactions were not noted. Anemia, leukopenia, or agranulocytosis did not develop. Two patients, not included in this series, on constant drainage because of prostatic obstruction, received sulfadimetine (4 Gm. daily) prophylactically for 30 and 33 days, respectively, without evidence of toxicity.

RESULTS

The results were evaluated on a clinical and bacteriologic basis after a follow-up period varying from 12 to 271 days. If the urine became sterilized and all symptoms disappeared, the final response was classified as cured. If, in mixed infections, the patients improved and the count of a bacterial strain was markedly reduced but not eliminated, the response was classified as good. If there was no bacteriologic improvement, or if the original flora disappeared but was replaced by other resistant strains, the response was classified as failure.

Twenty-seven of the 40 patients responded satisfactorily to sulfadimetine therapy, i.e., 24 were cured and 3 showed a good response. Twenty of these patients had failed to benefit from prior therapy, in 8 cases with penicillin, in 8 with penicillin and Aureomycin, in 2 with Aureomycin alone, in 1 with penicillin and Sulfamethazine and in 1 with Chloromycetin.

Of a total of 15 patients with infections which were resistant to Aureomycin, 10 responded to sulfadimetine therapy. Sixteen of the 24 bacterial

strains (5 to 8 strains of *B. proteus vulgaris,* 4 of 7 strains of *Ps. aeruginosa,* 4 of 4 strains of *Esch. coli,* 1 of 2 strains of *A. aerogenes,* 1 of 2 strains of paracolon bacilli, and 1 of 1 strain of *Streptococcus faecalis*) encountered in these 15 patients were cleared from the urine with sulfadimetine. The inferiority of Aureomycin in this group of patients was due chiefly to the well-known resistance of most strains of *Ps. aeruginosa* and *B. proteus vulgaris* to this drug.

Thirteen patients did not respond to sulfadimetine. The initial response was good in some of these but, as in Cases 10 and 24, the original flora was replaced by a resistant flora during therapy.

Of the 20 monovalent infections, there were 6 in which the urine could not be sterilized. Two were due to *Esch. coli,* 2 to *B. proteus vulgaris* and 1 each to *A. aerogenes* and *Ps. aeruginosa.*

Of the 20 mixed infections, the urine was sterilized in only 10. Three others showed clinical and partial bacteriologic improvement. The remaining 7 failed to respond.

Of the 67 bacterial strains found in the urines of the 40 patients, sulfadimetine eliminated 46 (17 of 22 strains of *Esch. coli,* 8 of 8 strains of *Staph. aureus* or *albus,* 4 of 5 strains of *A. aerogenes,* 2 of 3 strains of paracolon bacilli, 1 of 2 strains of streptococci and 1 of 1 strain of *diphtheroids Bacilli,* but only 6 of 15 strains of *Ps. aeruginosa* and 7 of 11 strains of *B. proteus vulgaris*).

DISCUSSION

Bacteria sensitive in vitro to sulfadimetine were always eliminated from the urine. Bacteria which resisted the drug in patients, or which appeared in the urine during therapy, were also resistant to the drug in vitro (Table III). There is, therefore, *a close correlation between the clinical effect of sulfadimetine and the in vitro sensitivity of the infecting bacteria to this drug.*

Failure to relieve obstruction in the urinary tract or the continued presence of an inlying urethral catheter always resulted in therapeutic failure, with persistence of the original flora or appearance of new strains.

Sulfadimetine is particularly effective against *Esch. coli, A. aerogenes* and *Staph. aureus.* Infections due to *Ps. aeruginosa* and *B. proteus vulgaris* are more refractory to sulfadimetine as well as to other sulfonamides and to available antibiotics. Sulfadimetine is more effective in monovalent than in mixed infections. Thus, sulfadimetine produced a satisfactory response in 13 of 20 patients with mixed infections for which NU-445 (Gantrisin), in our experience, is of little or no value.[3] It is, therefore, much superior to NU-445. Although somewhat less effective therapeutically, it is pharmacologically superior to Sulfamethazine* because of a much lower order of acetylation and greater ease in maintaining therapeutic concentrations of the drug in blood.

SUMMARY

1. Sulfadimetine is effective against a variety of gram-negative and gram-positive bacteria commonly encountered in urinary infections. In many in-

*The variable degree of conjugation of sulfamethazine requires frequent determinations of blood concentration in order to maintain effective blood levels.[6-9]

stances the drug possesses a greater antibacterial effect in vitro than other sulfonamides. It is often effective when antibiotics fail.

2. Sulfadimetine shows a low order of acetylation (about 10 per cent), and blood levels of 6 to 8 mg. per cent of free sulfonamide are easily maintained on 4 Gm. daily.

3. Clinical trial in 40 patients with urinary infections yielded a satisfactory response in 27. Improvement was observed in some patients with polyvalent as well as with monovalent infections.

4. There were no untoward reactions. With no attempt made to maintain an adequate daily fluid intake or to alkalinize the urine, no renal or hematopoietic toxicity occurred.

5. Apart from the notable lack of toxicity and the low order of acetylation, which recommend its use, sulfadimetine frequently proves more effective than other sulfonamides and antibiotics.

6. The in vitro sensitivity test is a reliable guide to the clinical antibacterial effectiveness of this drug.

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Case Reports

PERIVESICAL BLEEDING FOLLOWING HERNIORRHAPHY DEMONSTRATED BY CYSTOGRAPHY

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A "TEARDROP" deformity of the bladder by perivesical hemorrhage or urinary extravasation has been described following lower urinary tract trauma. The deformity may be seen with pelvic hemorrhage or in perivesical abscess above the levator ani muscles. Spasm or tetany of the detrusor urinae following trauma may also produce this deformity of the bladder.

CASE REPORT

A 22-year-old white man was admitted on Nov. 8, 1950, complaining of pain in the right inguinal region of three weeks' duration. Physical examination revealed a right inguinal hernia. On Nov. 13, 1950, a right inguinal herniorrhaphy was done under spinal anesthesia. The bladder was not dissected from the peritoneum. Twenty-four hours after operation, the patient complained of mild periumbilical pain which persisted for forty-eight hours. On the fourth postoperative night the pain increased in severity, shifted to the left lower quadrant, and was accompanied by anorexia and temperature of 101.4° F. The white blood count and urinalysis were within normal limits. Examination revealed tenderness, mild spasm, and slight rebound tenderness in the left lower quadrant. Bowel sounds were active. There was dullness to percussion two fingerbreadths above the symphysis pubis which persisted following catheterization. Flat and upright films of the abdomen revealed a moderate ileus. Cystogram (see Fig. 1) revealed a "teardrop" deformity of the bladder. Lateral films showed flattening of the anterior wall of the bladder. Antibiotics were given prophylactically. In forty-eight hours the patient was asymptomatic. On the seventh day following surgery the sutures were removed. The wound was healed. On the eleventh postoperative day a repeat cystogram (see Fig. 2) revealed the bladder returning to a more normal contour. One month later the cystogram was normal with the exception of elevation of the right (operative) side of the bladder (see Fig. 3).

A series of preoperative and postoperative cystograms was done on sixteen patients who underwent herniorrhapies. The only deformity noted was elevation of the bladder on the operative side. In cases of unexplained lower abdominal pain following herniorrhaphy or extraperitoneal operations of the lower abdomen, bleeding in the perivesical space should be considered as a cause of the pain. A "teardrop" deformity of the bladder when demonstrated

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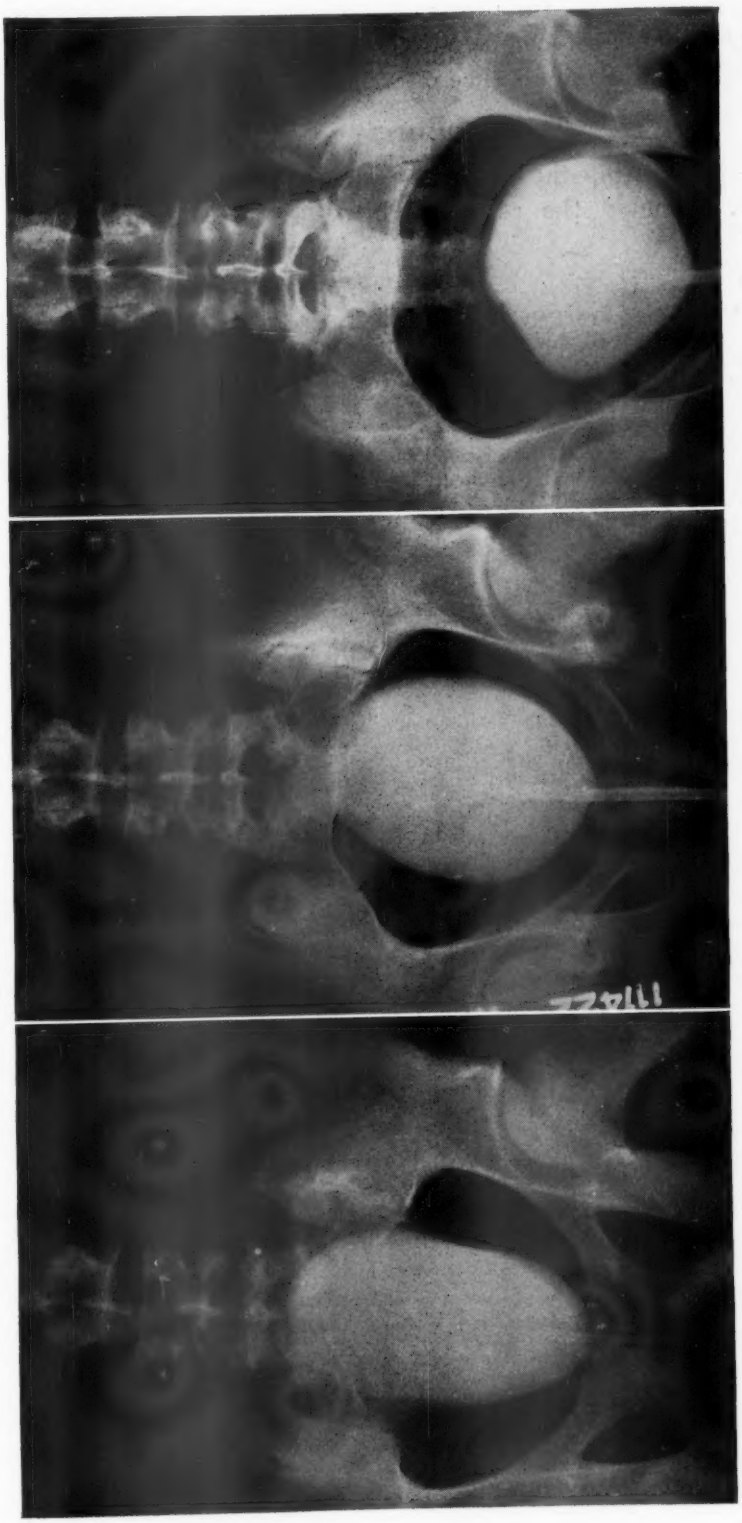

Fig. 3.

Fig. 2.

Fig. 1.

Fig. 1.—Cystogram, fifth postoperative day.
Fig. 2.—Cystogram, eleventh postoperative day.
Fig. 3.—Cystogram, thirtieth postoperative day.

by the cystogram, indicates the presence of fluid in the perivesical space. Conservative management is recommended for blood in the perivesical space, if it is not massive, and in the absence of infection.

SUMMARY

A case demonstrating the "teardrop" deformity of the bladder following herniorrhaphy, probably the result of bleeding in the perivesical space, is reported.

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INTUSSUSCEPTION OF THE SMALL INTESTINE PRODUCED BY METASTATIC RENAL CARCINOMA

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WHEN intussusception occurs in adults, an organic lesion can usually be found as the etiologic factor. About 75 per cent of the time tumors are responsible, of which 60 per cent are benign. Of those that are due to malignancies, very few have been metastatic. It is rare for hematogenous metastases to occur in the intestinal tract, and rarer yet for them to produce intussusception. Because of the rarity of these events, this case is reported.

CASE REPORT

P. B., a 41-year-old white man, entered Cook County Hospital on Feb. 11, 1951, complaining of abdominal pain, weakness, anorexia, and a weight loss of about forty pounds in five months. One week prior to entry he had intermittent epigastric cramping pain which occasionally radiated to his back. The pain might occur any time of the day or night, was unrelieved by any medication, but was occasionally alleviated by vomiting. There was never hematemesis nor abdominal distention. Since November, he had had intermittent periods of diarrhea and constipation, but the color of the stools maintained a normal brown. His past medical and surgical histories were negative. The family history was noncontributory.

On entry the patient was alert and cooperative and appeared chronically ill. The blood pressure was 115/50, and the pulse was 120. A soft systolic murmur at the apex of the heart was heard. There was some tenderness and a sense of fullness in the epigastrium and left upper quadrant of the abdomen. After some days a hard mass deep in the left flank was palpated. Peristaltic rushes occurred with the cramping pain. Stool examination revealed red-brown feces which were benzidine positive continuously. Palpable lymph nodes were present in the left anterior cervical chain. The hemoglobin was 34 per cent, red blood cell count was 2,100,000, white blood cell count was 17,500, with 75 per cent polymorphonuclears, 13 per cent band cells, 2 per cent eosinophiles, 7 per cent lymphocytes, and 3 per cent monocytes. The urine was acid with a specific gravity of 1.025 and was negative for albumin, sugar, acetone, cells, and casts. The blood Kahn test was negative. Nonprotein nitrogen was 32, total protein 6.0, total cholesterol 174, alkaline phosphatase 3.2, icterus index 4, thymol turbidity 1.7, cephalin flocculation 0, gamma globulin 0.82, and serum amylase 8 units on two occasions. A chest film revealed a normal cardiac shadow and an area of increased density overlying the right fifth anterior rib. A barium meal on Feb. 16 revealed a somewhat deformed duodenal bulb which was interpreted as a duodenal ulcer. A barium enema was negative. A repeat barium meal on March 3 showed a deformity of the duodenal cap, narrowing of the second portion of the duodenum, and displacement and dilatation of the upper jejunal loops.

During his hospital stay, the patient ran a febrile course with a temperature of 100° to 102° F. The symptoms remained unchanged except that there occurred two episodes of very severe abdominal distress accompanied by marked weakness, palpitation, sweating, and a fall in blood pressure. During these episodes he was given a total of 5,000 c.c. of whole blood, after which his hemoglobin was 73 per cent. He was transferred to a surgical ward on March 7, and exploratory laparotomy was performed.

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An orange-sized intraluminal mass of the jejunum was encountered which proved to be a chronic intussusception, the intussusceptum being led by a large polypoid mass (Fig. 1). This was resected, and end-to-end anastomosis performed. A more complete examination revealed that there were multiple tumor masses in the jejunum proximal to the one above (Fig. 2), and a retroperitoneal mass (Fig. 3). The ileum and colon seemed uninvolved. A six-foot segment of jejunum containing these tumors was resected. It contained fourteen tumor masses, some flat and infiltrating the entire thickness of the bowel, some polypoid; of the former, some were ulcerated. Microscopic sections studied from three polypoid tumors, three ulcerated tumors, and the retroperitoneal mass all revealed essentially the same microscopic picture (Fig. 4). The tumor tissue presented a variable pattern: solid sheets of cells in places, columns of cells elsewhere, and occasional attempts at glandular formation. The nuclei were large, hyperchromatic, extremely pleomorphic, and many mitotic figures were present. Large thin-walled sinusoids were noted (Fig. 5). A silver stain preparation showed no argentaffin granules, and a fat preparation no abnormal amount of fat.

The immediate postoperative course was uneventful. The patient began eating soft foods and passing stools. After a few days, the cramping abdominal pain recurred with occasional vomiting, and the stools became liquid and contained blood. It was soon impossible for him to retain food, and he became progressively more malnourished. He died on April 14, 1951. An autopsy was performed.

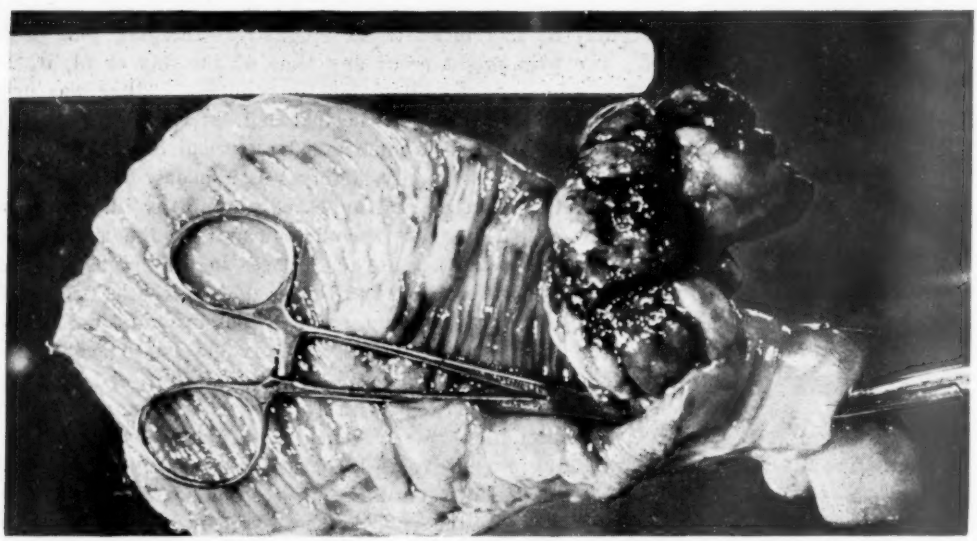


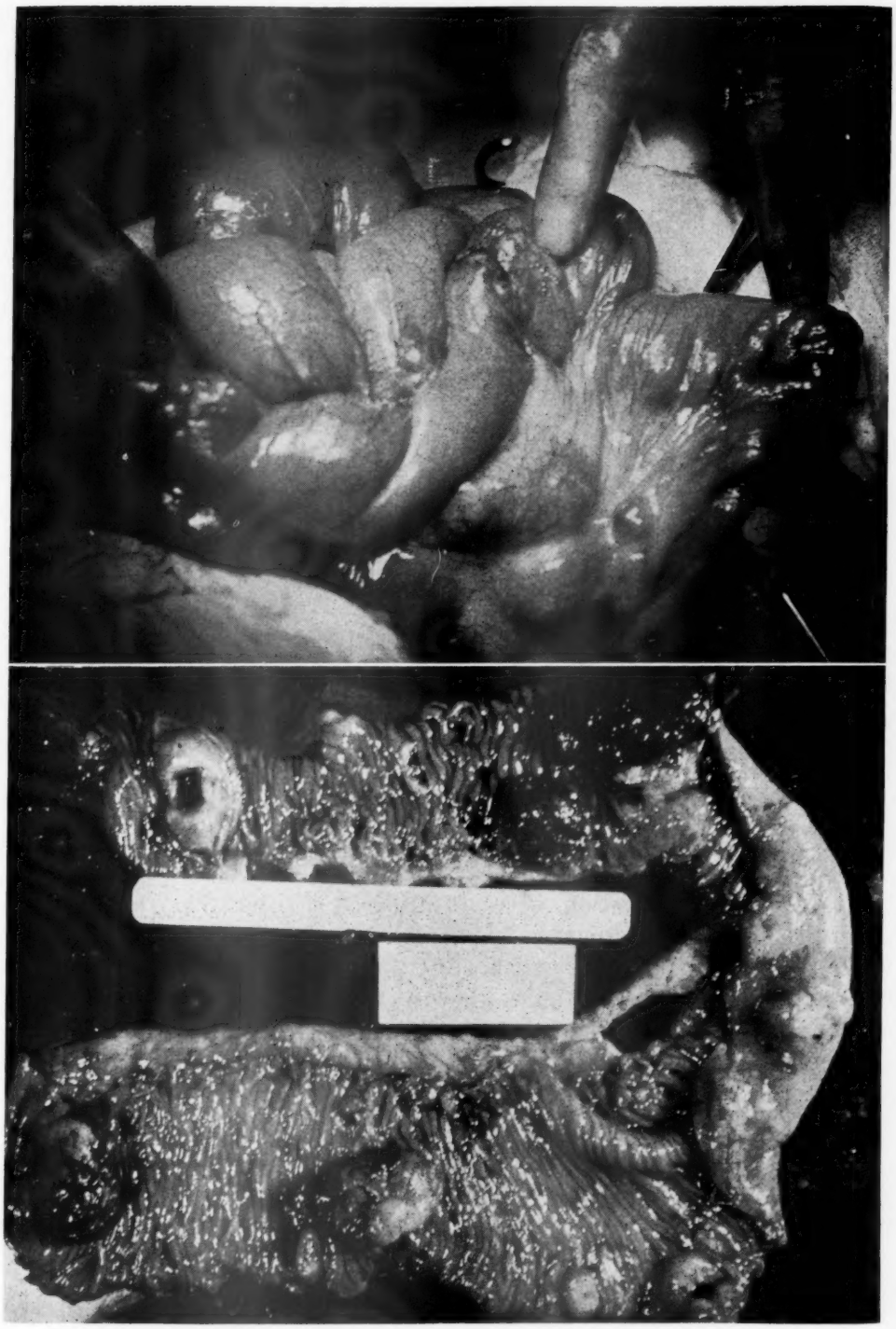
Fig. 1.—Resected specimen of jejunum which has been opened. A large polypoid mass is seen presenting as the intussusceptum in this chronic intussusception.

POST MORTEM

A 3 cm. tumor mass was found in the right lower lobe adjacent to the bronchus and invading its wall. Microscopic section revealed the tumor tissue to be replacing normal parenchyma and invading the mucosa of the bronchus, leading to ulceration.

Throughout the abdominal cavity were multiple, white, firm tumor masses. The liver and spleen were studded by several of these, measuring 0.4 to 2.0 cm. in diameter. Both adrenal glands were enlarged and the parenchyma was replaced almost completely by tumor tissue. Both kidneys had numerous tumor tissue implants, varying in size from 0.3 to 2.0 cm. In the lower pole of the right kidney there was a round tumor mass, approximately 1.5 cm. in diameter, firm and red-white in color, the center of which was slightly necrotic. Throughout the small intestine were numerous firm, white tumor nodules 0.8 to 1.5 cm. in diameter. Some were pedunculated while others were flat, being part of the mucosal surface. In the lower

A.



B.

Fig. 2.—Multiple tumors of the jejunum as seen (*A*), before resection and (*B*), after opening of the specimen after resection.

ileum was an annular ulcerating lesion which extended through the wall of the bowel and was visible on the serosal surface. In the jejunum were two points of anastomosis where segments of jejunum had been removed.

Histologically and cytologically the tumor tissue in each of the above organs appeared the same as that described above.

Fig. 3.—A large retroperitoneal metastatic mass.

COMMENT

At the time of operation, it was considered possible that this was a case of multiple primary carcinomas of the small intestine because of the numerous discrete pedunculated masses and because no other primary lesion was known. However, the microscopic studies showed that the tumor masses were consistently submucosal without any transition of normal mucosa into the masses at any place. From this and a more complete study afforded by the postmortem examination, it was decided that these represented metastatic carcinomas instead. The question arose whether the primary tumor was in the kidney or in the bronchus. There was a tumor nodule in the lower pole of the right kidney which was interpreted as a hypernephroma. In the right lower lobe of the lungs there was also a tumor nodule which appeared to invade the bronchus.

The microscopic examination of the various tumor nodules revealed an essentially uniform picture which was consistent with either an anaplastic bronchogenic carcinoma or with a primary hypernephroid carcinoma. While the pattern of metastases supports the former, the following histologic features support more the diagnosis of hypernephroid tumor: the wide sinusoids surrounded by tumor cells; the impression under low-power microscopy that the

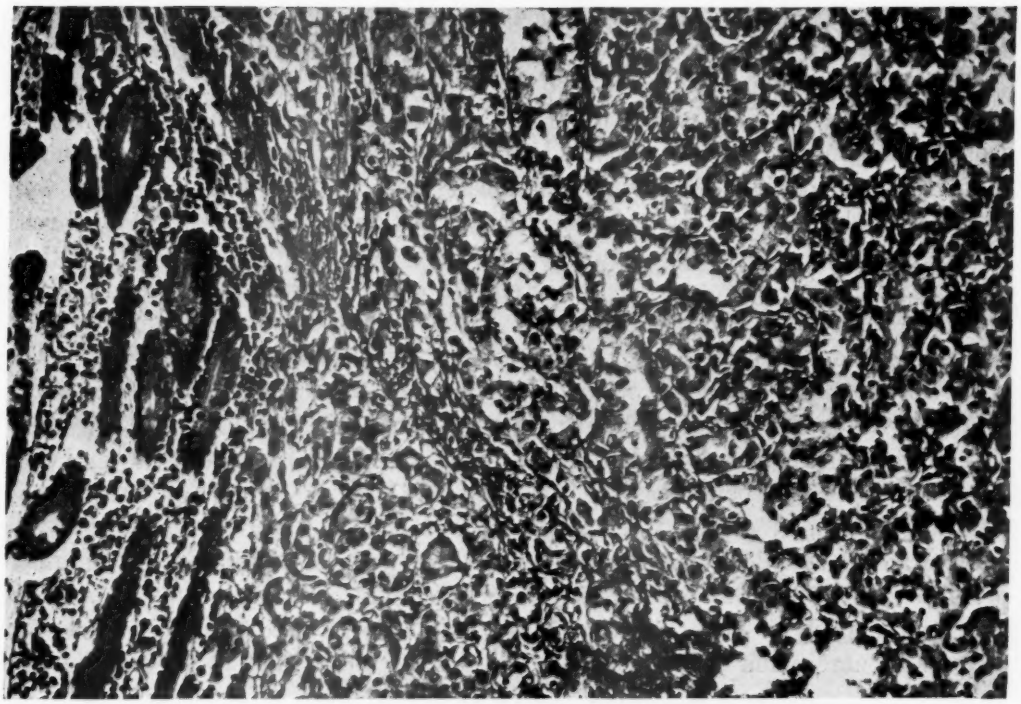


Fig. 4.—Microscopic section of tumor nodules under low power.

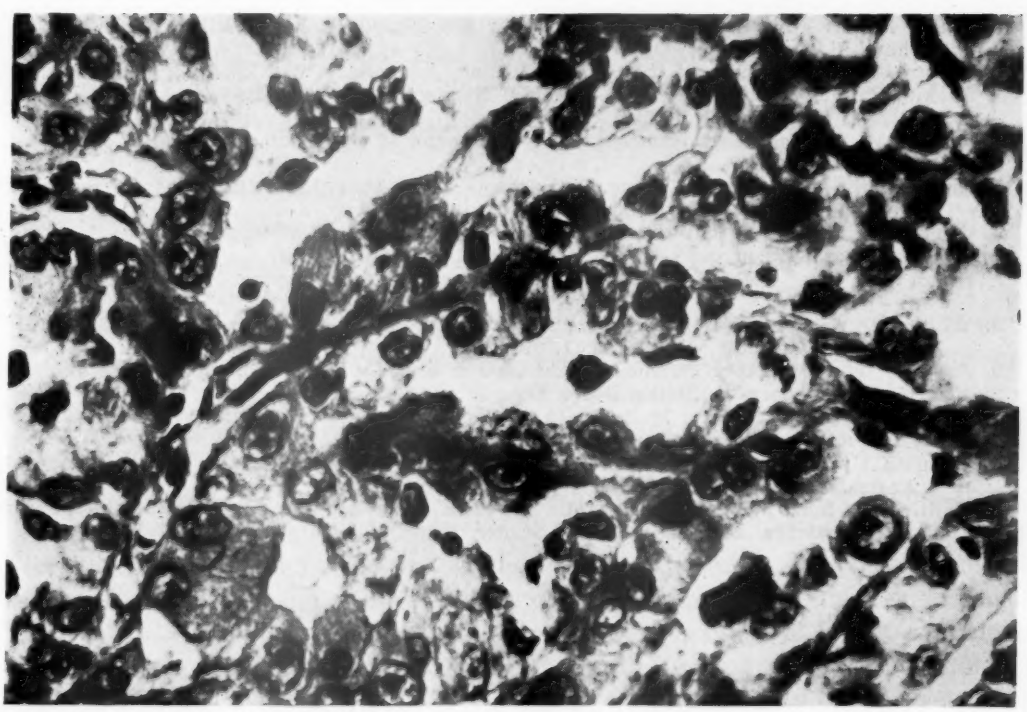


Fig. 5.—Microscopic section of tumor nodules under high power demonstrating the thin-walled sinusoids and hyperchromatic and pleomorphic cells.

bronchial wall was invaded by a peribronchial tumor nodule. Thus, it was decided that this was a case of hypernephroma of the kidney with metastases to the intestinal tract which produced intussusception.

Carcinoma of the small intestine is uncommon and metastatic carcinoma even less common. Willis[1] reported that in 323 cancer patients on whom he performed an autopsy, discrete blood-borne metastases to the intestines were found in eight (2.4 per cent). The primary lesions in these were the breast (four), thyroid (one), lung (one), pharynx (one), and reticulum cell sarcoma (one). From the literature he collected 135 cases of metastatic growth in the intestine, ten of which were from the kidney and 17 from the lung. While metastatic neoplasms of the small intestines are rare, a resulting intussusception is even more rare. Raiford[2] reported 88 cases of tumors of the small intestine in 11,500 autopsies and 45,000 surgical specimens of which 50 were benign and 38 malignant. In 23 per cent of these, intussusception had occurred, and most of these were in the benign group. Rankin and Newell[3] found that intussusception occurred in 17 per cent of 35 cases of benign tumors of the small intestine, while Rankin and Mayo[4] reported that of 55 cases of carcinoma of the small intestine only two (3.6 per cent) had intussusception.

In the past 35 years we have been able to find reports of eight cases of metastatic carcinoma to the small intestine which resulted in intussusception. One of these was from a hypernephroma,[5] one from a testicular sarcoma,[6] and six melanosarcomas.[7-12]

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CAROTID BODY TUMORS: REPORT OF REMOVAL OF TUMOR THOUGHT TO BE LARGEST RECORDED

CAROTID REMOVAL, HEMIPLEGIA, RECOVERY

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CAROTID body tumors are rare in comparison with other lesions in the neck, but over 300 have been reported since the first was removed by Riegner in 1880. Von Haller described the tumor first in 1743. Bibliography has been compiled by Lahey and Warren,[5] Pemberton and Livermore,[8] and others in appended references.

No record was found in the literature of successful removal of a tumor as large as the one reported here, and, though it is recognized that recording of limited observations may overburden the literature, departure from this rule is thought permissible if a chance of cure of even a single patient might be offered.

Anatomy.—The carotid body is oval in shape, about ½ cm. in diameter, and reddish brown in color. Location at the bifurcation of the common carotid artery establishes the reason for its technical surgical significance. The possible effect of ligation of the common carotid artery and the importance of the surrounding anatomy, such as the close relationship of the vagus and other cranial nerves and the jugular vein, the brachial plexus, and the esophagus, make the removal of a tumor the size of the one reported most difficult. However, technical difficulty for the surgeon is not taken as a contraindication for operation (Figs. 3 and 4).

Microscopically, the normal carotid body is covered by a fibrous capsule, continuations of which extend into the organ as septa. There are cuboidal cells of little cytoplasm and oval nuclei with a nucleolus, mainly comprising the parenchyma. Ganglion cells are seen (Figs. 1 and 2).

Pathology.—Grossly, tumors appear much as the one reported, firm to palpation, gray to brown on section, with a fibrous capsule branching into fibrous septa. Microscopically, the picture seems to be mainly of hyperplasia of the normal gland, as it seemed in this tumor. There have been reported instances of malignancy, extension occasionally, metastasis very rarely. There may be difficulty in differentiation from carcinoma of other origin and, as these tumors are usually benign, this differentiation is important in relation to the type and extent of operation. Because of the location and inherent dangers of removal, this is another instance where the pathologic diagnosis of benign tumors with its inference of ease of removal and safety for the patient is out of proportion to the seriousness of prognosis and difficulty of treatment. "Malignant by position" might be thought to be applicable as far as difficulty of removal is concerned.

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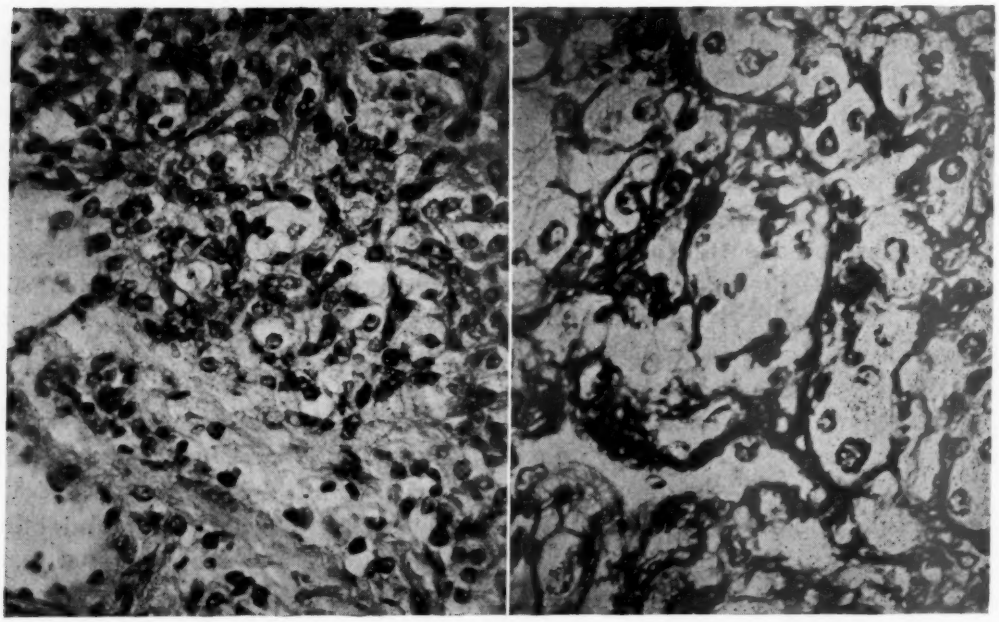
Diagnosis.—Differential diagnosis requires the elimination, among others, of a solitary metastatic node in the superior deep cervical chain, an inflammatory lymph node, a branchial cleft cyst, a lateral thyroid mass, and a vascular anomaly, such as an aneurysm. The last is not usually of important concern, considering previous reports, but in this patient it was one of the most likely possibilities. Two previous explorations elsewhere gave the opinion that this was an arteriovenous aneurysm.



A. *B.*

Fig. 1.—*A*, Photomicrographs of tumor. Microscopic pattern is typical of carotid body tumor with uniform cells. No mitoses. Extreme vascularity.

B, Reticulin stain, demonstrating that reticulin encloses groups of cells, characteristic of a paraganglioma. Does not reduce chrome salts. (Personal communication from Dr. L. V. Ackerman, Department of Surgical Pathology, Washington University School of Medicine.)

CASE REPORT

Report of Removal of Excessively Large Tumor, Thought to Be Larger Than Any Previously Recorded; Removal of Carotid System; Hemiplegia With Recovery.—A 62-year-old woman, twenty-one years previously, noticed a small, painless mass in the left side of the neck. The mass continued to enlarge slowly, but without pain or discomfort, except for complete distortion and unsightliness of the whole side of the neck from the clavicle to the jaw. Two exploratory operations had been performed elsewhere without completion, as aneurysm had been thought to be present and to preclude removal (Fig. 2, *A*).

Physical examination was negative except for a huge tumor occupying the entire left side of the neck. It measured about 10 by 15 by 12 cm. The mass felt warm, but was not red or particularly tender. There was some expansile dilatation but no thrill. Auscultation revealed a definite bruit, but there was not a real to-and-fro type of murmur. Mouth, nasopharynx, chest, blood pressure, blood, and urine were thought to be normal. Serology was negative.

Impression from the two previous explorations was of some sort of vascular anomaly in the neck, possibly an arteriovenous aneurysm, but more likely a vascular pattern associated

with some underlying tumor. Needle punch biopsy was considered too dangerous in this very vascular tumor, and re-exploration was thought to be indicated.

Operation.—To obtain exposure of the entire side of the neck necessary for the possible removal of this large tumor and to protect the normal structures, the usual incisions and reflections of skin flaps for a complete neck dissection were made. It was immediately apparent that biopsy was not safe until numerous, large (averaging about 1 cm. in diameter) veins overlying the tumor were ligated. The internal jugular vein was ligated just above the clavicle where it could be isolated below the tumor mass. The edges of the tumor were slowly freed near the cornu of the hyoid anteriorly, at the trapezius and levator scapulae posteriorly, then along the body and angle of the jaw from above. There was no question that this was a solid tumor completely enveloping the jugular vein and common carotid artery with both the external and internal branches extending from the above-described limits. The vagus nerve was adherent to the posterior and inferior portions of the tumor, but it was possible to preserve it by careful dissection. The vagus actually was used as a guide, its being the most consistently distinguishable anatomic element in an enmeshing group of huge vessels and an attendant severe hemorrhage.

A. *B.*

Fig. 2.—*A,* Large pulsating carotid body tumor. *B,* Minimal deformity following removal of tumor. Patient returned to former occupation.

It was presumed that an enveloping tumor of this size probably had caused gradual constriction of the common and internal carotid arteries by its growth, and, because life could hardly continue to be compatible with this tumor, ligation of the common carotid artery was performed. The tumor was removed by leaving a margin of normal tissue over the capsule, continuing from below, ligating the ascending pharangeal, superior thyroid, lingual, external maxillary, occipital, and posterior auricular arteries with the associated veins. The hypoglossal nerve was found entering the mass so that it necessarily was removed

in the tumor. The internal jugular vein was ligated above, just below the bulb. The only points of attachment were then the internal and external carotids which were doubly ligated, in addition an artery clamp being left on the internal carotid, since the pedicle for ligation was so short just under the foramen lacerum.

During this procedure there was little fluctuation in the pulse and blood pressure, any change being prevented by the administration of 2,000 c.c. of whole blood. The skin flaps were then closed over the defect and around the artery clamp. A stabilizing, firm pressure fixation dressing was applied to promote healing, and surgical waste was held securely and comfortably by gauze rolls around the head and strapped to the chest and back. This dressing is a part of any extensive neck dissection and is thought to be of notable importance.

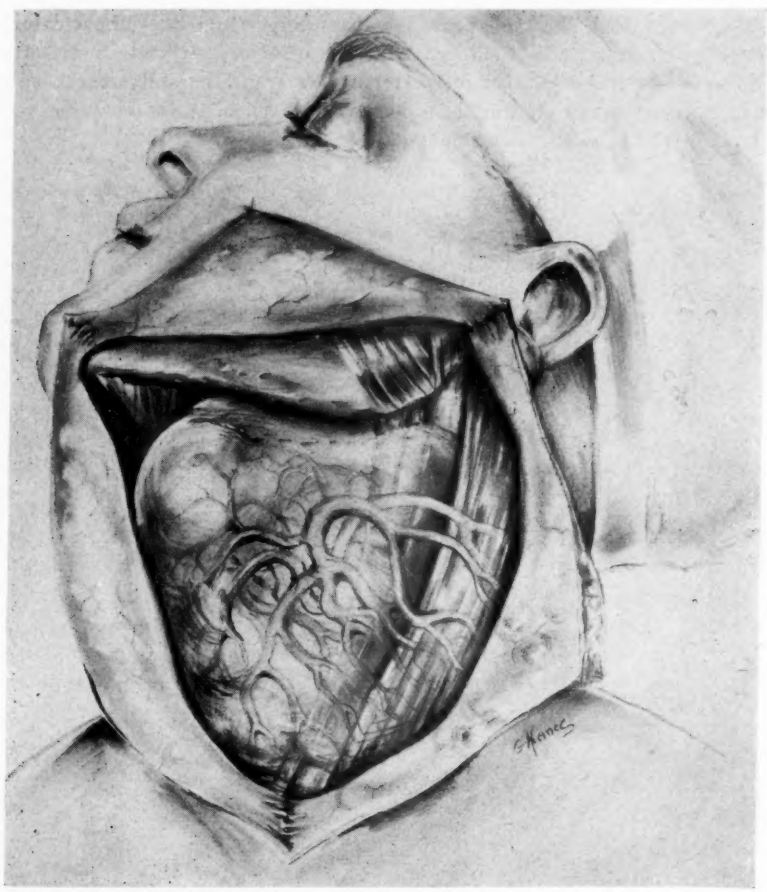


Fig. 3.—Diagrammatic drawing of tumor involved in carotid system, covered with numerous, large branches of the jugular vein, encompassing the twelfth cranial nerve, and distorting other normal structures in the neck, including the vagus nerve. Protection of these structures by exposure with wide reflection of skin flaps. Field sufficient for complete neck dissection if thought necessary at time of operation.

Postoperative Progress.—In order to avoid a propagating clot in the circle of Willis, anticoagulant therapy was started and continued to the fourth postoperative day on consultation with Dr. Edward Reinhard.[8]

The evening of operation the patient was quite drowsy but responded to her name. She would not move the right arm or leg, but the deep reflexes in the extremities were always present. On the first postoperative day, she was more alert, recognizing and calling the names of her family and friends. There was some difficulty of respiration on the following day so that the artery clamp was removed, allowing for better head position and un-

obstructed respiration. Alertness continually improved and on the third postoperative day the patient began to move the right arm and leg. In one week she walked around the bed, could feed herself, and on the tenth postoperative day wrote a letter. Mental improvement paralleled motor progression. Two weeks following operation, no longer needing a dressing, the patient walked out of the hospital, ready the following week to return to her former occupation of clerk.

The satisfactory outcome was due in a large measure to preparation for operation, assistance during the surgical procedure, and postoperative care by the house staff, and to the anesthetists on this service.

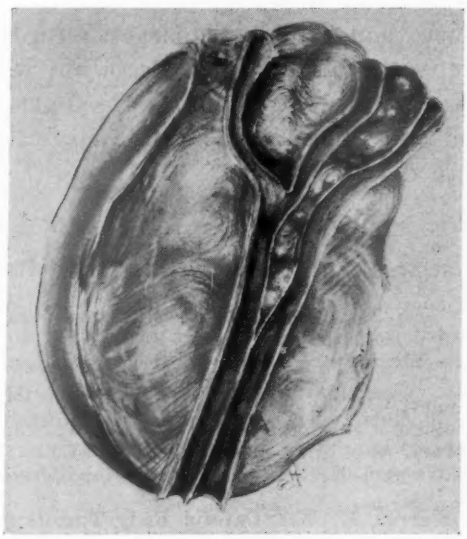


Fig. 4.—Diagrammatic drawing of cross section of tumor following removal. Carotid system and jugular vein completely surrounded by tumor, making their removal obligatory for best chance of cure. Compression of common and internal carotid by the tumor probably lessened effect of ligation at operation.

COMMENT

The surgery of the carotid body tumors includes surmounting the technical difficulties of the removal itself, and the evaluation of, and allowing for, the requirements of the circulation of the brain. In this instance it had been thought that the complete envelopment of the carotid system had performed its own partial ligation. This may be seen in some aneurysms as far as the effect of reduced peripheral blood flow is concerned. This possible occlusion might be determined by direct dissection through the tumor for the full exploration of the contained artery, but the excessive hemorrhage from the excess of dilated vessels prevented it here.

Preliminary partial occlusion can be carried out by any method preferred in some instances, if it is thought that the carotid system may have to be removed, but this could not have been done here with safety because of the other excessive vessels present, and the extensive dissection that would have been necessary.

It is obvious that ligation of the internal or common carotid, without preliminary partial occlusion, may be productive of paralysis or death, especially in older patients, and an acute balance has to be developed and maintained in

the detail of removal of the tumor for the patient to remain alive and unparalyzed. It happened in this patient that the size of the tumor itself was such as to make the patient accept the possibility of fatality or paralysis before operation.

Possibilities of response to radiation are not positively known because of the few observations. The tumor is so cellular that interstitial radiation might be considered in some instances, if the microscopic diagnosis were available.

SUMMARY

A carotid body tumor, thought to be the largest recorded, was removed along with the carotid system, with transient hemiplegia but with complete recovery, so that the patient walked out of the hospital on the fourteenth day. References to other experiences and reviews are made and the surgical problems of adequate cerebral circulations are discussed.

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SCALENUS ANTICUS SYNDROME PRECIPITATED BY AN ATTACK OF PLEURISY

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IN A fairly large experience with the surgical treatment of the scalenus anticus syndrome,[1] and in the literature pertaining to this and related syndromes, no case similar to the one reported here was encountered. A 46-year-old white woman without cervical ribs had had no clinical symptoms of vascular or nerve compression in the upper extremities until an attack of pleurisy with radiation of pain to the right shoulder. Almost immediately following this attack she experienced the full-blown picture of a right scalenus anticus syndrome.

Mrs. T. L. (ABH No. 49-1317), 46 years old, was first seen at the clinic May 9, 1949, complaining of severe pain in the right lower abdomen of ten years' duration, with severely progressive dysmenorrhea forcing her to take to her bed with each menstrual period. Operation on May 16, 1949, revealed old pelvic inflammatory disease with numerous adhesions and bilateral hydrosalpinx. There was no evidence of endometriosis. Presacral neurectomy and bilateral salpingectomy were followed by uneventful recovery and gratifying amelioration of symptoms. She returned on March 27, 1951, for treatment of varicose veins, and on March 28 underwent bilateral high saphenous ligation and stripping of each saphenous vein to the ankle. On April 1 she complained of severe right-sided pleuritic chest pains radiating to her right shoulder. Chest x-rays revealed no evidence of pulmonary infarction or pneumonitis and there was no cough or hemoptysis. Her chest was clear to auscultation and percussion. Her pleurisy subsided over the next few days and she was discharged on April 4, 1951. She returned postoperatively for the removal of stitches from her incisions which healed well. From the time of her first postoperative visit on April 11, she complained of numbness and tingling in her right arm which was accentuated by drooping of the right shoulder and which awakened her from sleep. She stated that these symptoms developed a day after the onset of her pleurisy. Repeated Adson tests revealed complete obliteration of the radial pulse when her right arm was held horizontally with her head turned to the left. Cyanosis and marked tingling pain in the fingers and right hand developed rapidly on maintenance of the arm in this position. Subsequently blanching of the fingers and hand occurred. There was no sensitivity to cold or other symptoms of Raynaud's disease or Raynaud's syndrome.[2] Palpation over the right scalenus anticus muscle produced local pain, whereas the region of the left scalenus anticus muscle was not tender to palpation. Adson's vascular test on the left side was negative and there were no symptoms on the left. X-ray examination was negative for the presence of cervical rib. Because of the progressive severity of symptoms, right scalenotomy was performed on June 18, 1951. This operation was followed by an uneventful convalescence and complete relief of symptoms. The Adson vascular test is now negative on the right side.

DISCUSSION

The etiology of the scalenus anticus syndrome with or without the presence of cervical ribs, as first described by Murphy[3] and Naffziger,[4] is generally

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ascribed to mechanical and traumatic factors. When a cervical rib is present the activity and freedom of movement of the subclavian artery and brachial plexus are restricted. Unusual occupations involving the necessity for prolonged hyperabduction of the arms in younger subjects and sagging of the shoulders due to advancing age or carrying of heavy loads may place sufficient stress on the scalene muscles to produce hypertrophy. Such hypertrophy may be sufficient to cause compression of the subclavian artery or brachial plexus, particularly if the floor of the posterior triangle is small to begin with. Contraction of the scalenus anticus muscle elevates the first rib into which it is inserted, a cervical rib if one is present, or the adhesions and bands which sometimes exist between enlarged transverse cervical processes or a rudimentary cervical rib or the first rib. Continued trauma to the subclavian artery by such contraction and pressure may cause the adhesions about the artery which have been ascribed to thrombosis of the vasa vasora by Adson[5] and others. Resultant inflammatory reaction accounts for the tenderness of the scalenus anticus muscle described by Gage[6] which is so commonly encountered. Such tenderness can be temporarily alleviated by local nerve block as suggested by Ochsner, Gage, and DeBakey,[7] and this forms the basis for a test in selecting patients for operation which is second only to the vascular test of Adson.

In the case reported, the pathogenesis is a matter of some speculation. From the anatomic standpoint it is not difficult to imagine the path of nervous reflexes set up originally by inflammation of the diaphragm and ending ultimately in spasms of the scalenus anticus muscle.

This muscle is supplied by twigs from the anterior primary rami of the lower five or six cervical nerves. It will be recalled that the phrenic nerve arises chiefly from the fourth cervical nerve with additional roots from the third and fifth cervical nerves. There is thus the opportunity for afferent impulses to be transmitted in cervical reflex centers to nerve fibers supplying the scalenus anticus muscle. There are three other possible explanations, one being the direct contact between the phrenic nerve and this muscle as the nerve courses over its anterior surface beneath the fascia. Another factor to be considered is that the cervical plexus itself which is formed by the anterior primary rami of the upper four cervical nerves is connected by a slender branch that descends from the fourth to the fifth, thus connecting it to the brachial plexus. Such a relationship might be the cause of paresthesia and other phenomena along ulnar, median, and radial nerve distribution.

The final possibility is that sympathetic nerve stimulation in the upper extremity may result from impulses in the phrenic nerve. Each anterior ramus of cervical nerves receives a gray ramus communicans from the superior cervical ganglion of the sympathetic trunk. These anterior rami of the lower four cervical nerves, together with the greater part of the first thoracic nerve, form the brachial plexus. They each receive a gray ramus communicans, those for the fifth and sixth derived from the middle, and those from the seventh and eighth from the lowest cervical ganglion of the sympathetic trunk.

Such sympathetic stimulation in the upper extremity would be manifested by coldness, cyanosis, hyperhidrosis, and other vasospastic phenomena.

In the case reported, the most prominent features of the symptom complex are related to scalenus anticus muscle compression of the subclavian artery and the picture was not predominantly that of vasospasm or peripheral nerve paresthesia. Complete numbness of the hand and forearm occurred concomitantly with obliteration of the radial pulse during performance of Adson's test prior to scalenotomy.

SUMMARY

The scalenus anticus or Naffziger's syndrome is described in a patient who first developed symptoms in the right upper extremity after an attack of pleurisy in the right chest with referral of pain via the phrenic nerve to the right supraclavicular area. The pathogenesis of the syndrome has afforded some speculation regarding reflex stimulation of the cervical nerves with resulting tenderness and spasm of the anterior scalene muscle. Scalenotomy has resulted in complete relief of symptoms and a negative Adson's test. This case illustrates that factors other than mechanical and traumatic mechanisms may sometimes give rise to the scalenus anticus syndrome.

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UNILOCULAR CERVICAL CYSTIC HYGROMA

Report of a Case With Attachment to the Thoracic Duct

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CYSTIC hygroma represents a congenital endothelial-lined cyst. Although the lesion has been reported in various sites, it is estimated by Gross and Goeringer[2] that approximately four-fifths of cystic hygromas occur in the cervical region. The most common location in the neck is the posterior triangle in or near the supraclavicular space. The mass is of variable size, nontender, soft, compressible, and transilluminates light. The cyst may be unilocular or multilocular, and contains a colorless or clear yellow fluid. Microscopically, the cyst is lined by flattened endothelium, and the wall consists of connective tissue in which islets of lymphocytes are found. The method of extension of large cystic hygromas by means of pseudopodial projections of endothelial columns which eventually acquire a lumen is described by Goetsch.[1]

Cystic hygroma is usually noted at, or soon after, birth. Gross and Goeringer[2] found that 90 per cent occurred within the first two years of life. However, initial occurrence in adolescent or adult years has been reported.

The condition is relatively uncommon. Vaughn,[5] in 1934, collected 155 cases from the literature. Since that time the only sizable presentations have been those of Goetsch,[1] in 1938 (12 cases), and Gross and Goeringer,[2] in 1939 (27 cases).

We believe the present case report is of interest in that it demonstrates a direct connection between a unilocular cervical cystic hygroma and the thoracic duct.

CASE REPORT

A. L. W. (B.H. No. 30181-49).—The patient was a 14-year-old Negro girl admitted because of a soft nontender mass in the left side of the neck, first noted six weeks prior to admission, at which time the patient complained of a stiff neck. The mass had been constant and had increased slightly in size. It was not painful and had not produced pressure symptoms referable to respiration or deglutition. There was no change in size after eating.

Past history revealed frequent attacks of tonsillitis and sinusitis for which the patient had been hospitalized on one occasion. She had had pertussis at the age of 12 years.

Family history was noncontributory and there was no history of similar lesion in the parents or siblings. The systemic review was essentially negative.

On physical examination the patient was found to be a well-developed, well-nourished adolescent Negro girl. In the posterior triangle of the left neck, just above the clavicle, was an oval, soft, cystic, subcutaneous mass measuring 4 cm. in diameter, which appeared

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to extend into the deeper tissues of the neck for an indeterminate distance. The mass was not tender, did not pulsate, and there were no changes in the overlying skin. The mass transilluminated light poorly. Pressure on the mass caused it to decrease in size. The remainder of the physical examination was negative.

Laboratory examination revealed a hemoglobin of 11.9 Gm. and a leukocyte count of 7,500. The urine contained a faint trace of albumin. Roentgenogram of the neck revealed

Fig. 1.—Preoperative photograph illustrating mass in left supraclavicular region.

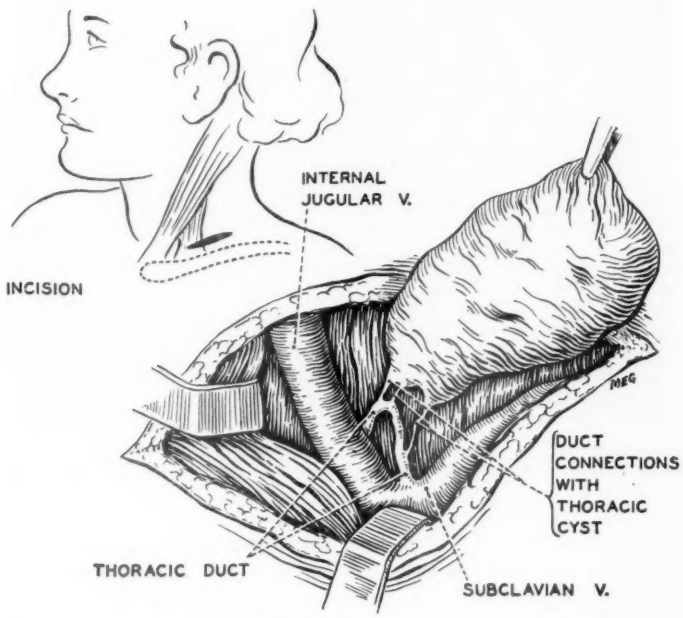

Fig. 2.—Drawing at operation showing connection of the cyst to the thoracic duct by means of three patent channels.

a soft tissue swelling in the posterior triangle of the left neck. The chest x-ray examination was negative.

Course.—The mass was aspirated and approximately 20 c.c. of milky fluid obtained. A definite decrease in size was noted following aspiration. At operation a thin-walled cyst containing chylous fluid was found presenting posterior to the sternocleidomastoid muscle. The cyst was loosely attached to the surrounding fatty and areolar tissues from which it was easily separated. The cyst extended to the base of the neck where it was connected to the thoracic duct by three channels, each of which measured approximately 2 by 3 mm. in diameter. These channels joined the thoracic duct just before the latter structure entered the subclavian vein. The fluid in the thoracic duct, the connecting channels, and the cyst was grayish white in color. The connecting channels were ligated and the cyst excised without interrupting the thoracic duct. Approximately 10 c.c. of fluid were found in the cyst, the major portion of its chylous contents having been removed by aspiration the preceding day.

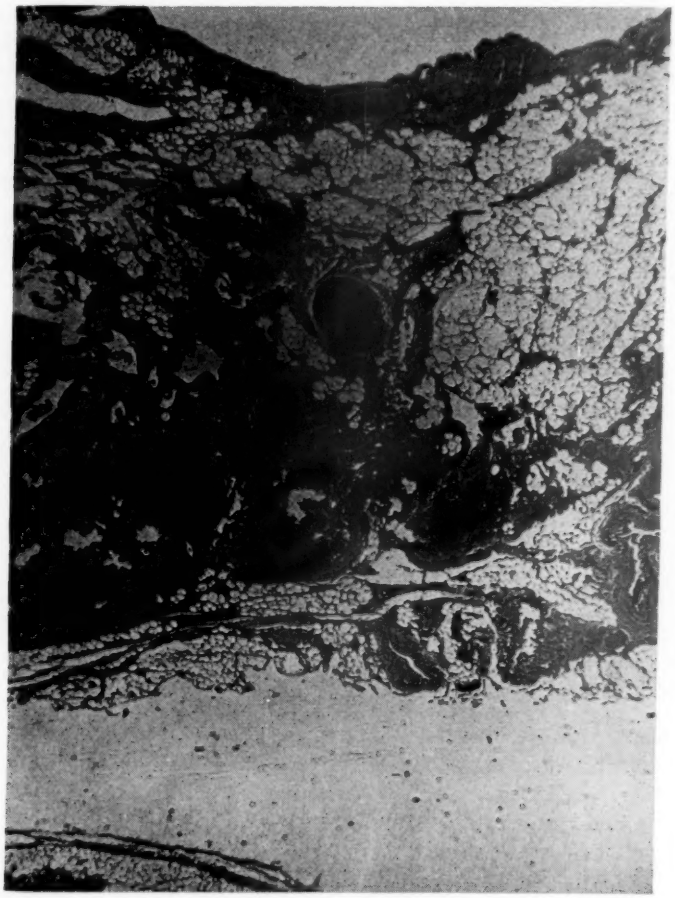

Fig. 3.—Photomicrograph of specimen showing endothelial lining, connective tissue wall containing scattered collections of lymphocytes, and adipose tissue of the fetal type. (Hematoxylin and eosin, ×100.)

Pathologic examination revealed a cyst measuring 6 by 4 by 0.3 cm. and lined with a glistening membrane. In the wall several small cystic areas were noted. Microscopic examination showed the cyst wall to be made up of edematous connective tissue and small amounts of smooth muscle. In a few areas a flattened endothelial-like lining was seen. In several areas collections of sinusoidal lymphatic channels were noted extending from

the cyst cavity, through the wall, to an area of lymphoid infiltration surrounding the cyst. The adipose tissue around the cyst was of the fetal type. The pathologic diagnosis was lymphatic cyst.

DISCUSSION

Two theories have been proposed to explain the embryogenesis of the cervical lymphatic system. Huntington, cited by Arey,[3] believes the system originates in the mesenchyme as endothelial-lined spaces which eventually ramify and coalesce to form lymphatic channels and, at an early stage, the paired jugular lymph sacs. Opposed to this view is Sabin,[4] who feels that the jugular sacs are derived as endothelial-lined projections from the jugular vein. He further postulates that from these primitive sacs lymphatic channels take origin and spread to the head and neck.

Irrespective of mesenchymal or venous origin, paired lymphatic sacs are to be found in the region of the jugular vein in the seven-week embryo. The lymphatic channels of the head and neck connect with these sacs. The jugular sacs eventually gain connection with the venous system by means of the thoracic duct on the left and the lymphatic duct on the right.

The present case illustrates connection of the hygroma to the thoracic duct by means of three patent channels, and probably arose as an embryonic rest which retained its original connection to the thoracic duct (i.e., jugular sac).

CONCLUSIONS

1. An unusual case of unilocular cervical cystic hygroma attached to the thoracic duct occurring in a 14-year-old girl is presented.

2. The embryogenesis of the cervical lymphatic system and its relation to the present case is discussed.

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PRIMARY LEIOMYOSARCOMA OF THE LUNG TREATED BY PNEUMONECTOMY

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THE incidence of leiomyosacroma is very low and as a primary lung tumor it is extremely rare. A search of the literature revealed only two case reports pertaining to this subject. We believe that the case to be reported is the first to be treated successfully by pneumonectomy.

CASE REPORT

V. R., St. John's Episcopal Hospital No. W1348, a white man, age 52 years, was admitted on Feb. 22, 1950. His complaints were pain in the right chest, cough, night sweats, and six pounds weight loss. Past history revealed only that he smoked two packs of cigarettes daily.

The only contribution of the physical examination was the finding of harsh expiratory breath sounds, heard over the right chest, superiorly. Other findings were not significant.

Laboratory data was within normal limits. Sputum examination was negative for tuberculosis.

Roentgenograms of the chest showed a dense opacity in the region of the right upper lobe. The V-shaped appearance suggested atelectasis (Figs. 1 and 2).

At bronchoscopy the carina was distorted and deviated to the right and grossly widened. The orifice of the right upper lobe was not visualized. The mucosa in the area was red and indurated. Cytologic examination of secretions was negative for tumor cells.

It was felt that the patient had a carcinoma of the right upper lobe which, in view of the bronchoscopic findings, did not seem resectable. An aspiration biopsy was done under fluoroscopic guidance but this was also negative for tumor cells. An exploratory thoracotomy was advised to establish a pathology diagnosis.

A thoracotomy was performed on March 20, at which the right upper lobe was found to contain a small tumor in close proximity to the hilum and the rest of the lobe was found to be atelectatic. A few small soft nodes were palpated in the mediastinum. A total pneumonectomy was necessary to remove the tumor. The convalescence was uneventful. At the present time he is well and free of disease.

Pathology.—The pathology report* was as follows:

Gross: The bronchus of the right upper lobe was occluded by a projecting fingerlike nodule which filled the upper lobe bronchus immediately distal to the line of resection. The nodule presented a piece of tissue 5 mm. in diameter at its proximal end and gradually increasing to a diameter of 1.2 cm. over a distance of 1.7 cm. in length. On incision of the upper lobe bronchus, considerable quantities of thick tenacious mucoid material escaped. The mass was found to originate from between the anterior and superior segmental bronchial orifices which were straddled and occluded. The base of the mass occupied an area of 1.5 sq. cm. The protruding nodule was freely movable. The base was fused with the bronchial mucosa and was poorly defined. The tumor was soft in consistence. External surfaces were pinkish gray and pearly white mottled by bright red and dark, reddish purple foci 1 to 3 sq. mm. in area. On section, the tumor was soft in consistence and had homogenous, pale, pearly white, moist, glazed cut surfaces (Fig. 3).

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*By Dr. Raymond Gettinger.

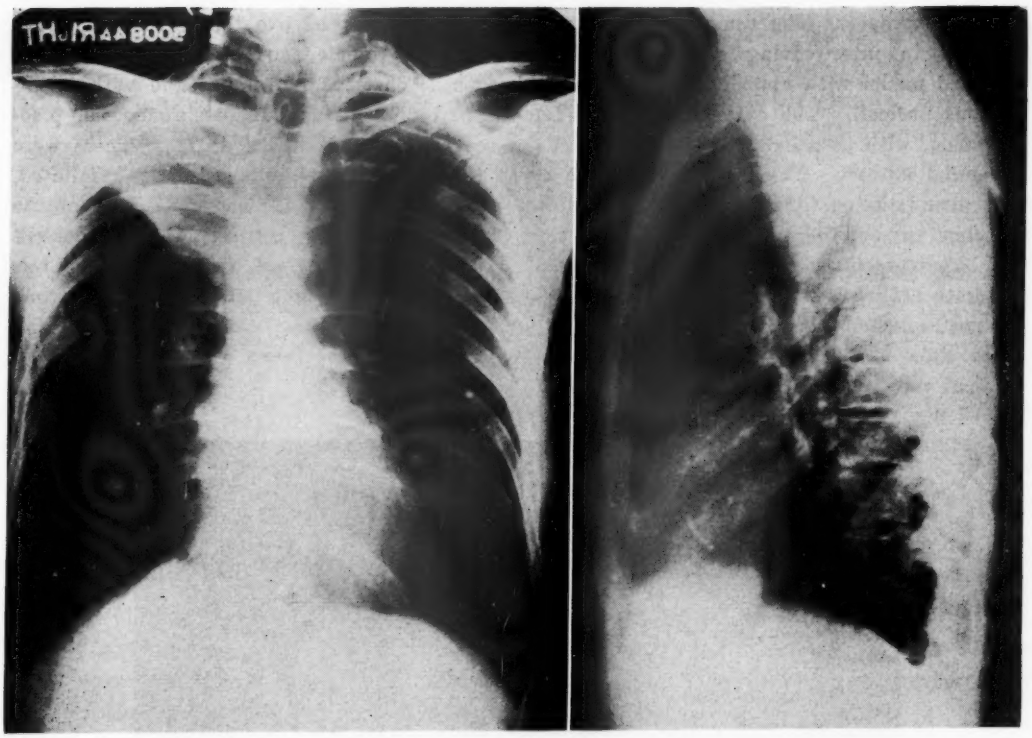

Fig. 1. Fig. 2.

Fig. 1.—Posteroanterior roentgenogram of chest revealing atelectasis of right upper lobe.
Fig. 2.—Lateral roentgenogram of chest showing wedge-shaped density of upper lobe.

Fig. 3.—Photograph of opened right main bronchus. Tumor occludes the apical and posterior bronchial orifices. Clamp indicates orifice of anterior segment. The base of the mass is directly below the point of the instrument.

Microscopic: The tumor was composed of aggregations of ovoid and fusiform cells arranged in interweaving sinuous bundles. They had rounded, ovoid, and occasionally lobulated nuclei with abundant fine to coarse basophilic chromatin granules and with inconspicuous nucleoli. The cytoplasm was acidophilic and filamentous. Hyperchromatism, pleomorphism, with occasional bizarre giant cells were evident to moderate degree. There were occasional mitoses. The tumor extended beneath the mucosa which was partially exfoliated, and beyond the cartilage of the bronchus into the subjacent stroma. The epithelium of the bronchus surrounding the tumor shows squamous metaplasia with considerable enlargement and hyperchromatism of many of the cells. Basal layers were well defined. There was moderate infiltration of polyblasts through the stroma. The adjacent pulmonic tissue beyond the peribronchial fibrous stroma was devoid of atypical cells. The tracheobronchial lymph nodes showed considerable anthracosis and moderate fibrosis. There was no evidence of atypical cells (Fig. 4).

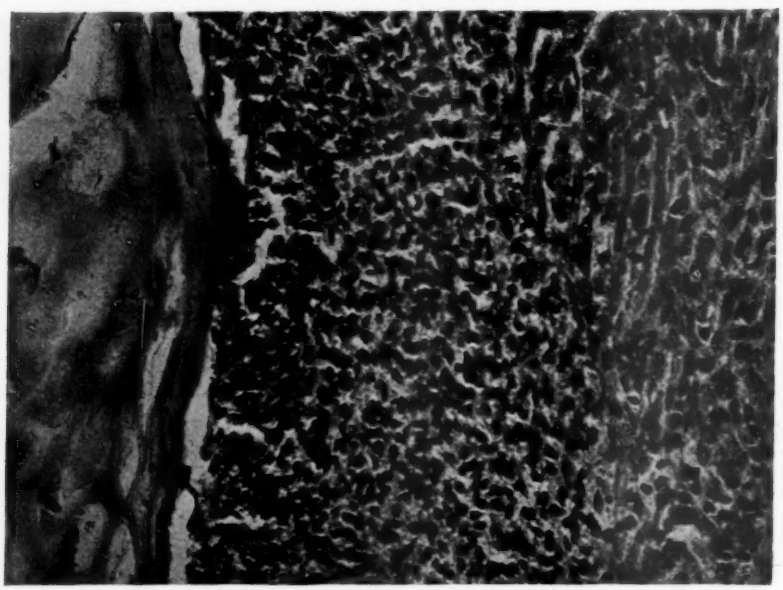

Fig. 4.—Photomicrograph of specimen showing the tumor adjacent to bronchial cartilage.

COMMENT

The paucity of reported cases of leiomyosarcoma of the lung makes it difficult to comment on this case. Despite the increased interest in pulmonary diagnosis as evidenced by routine chest surveys, greater numbers of diagnostic bronchoscopies, and cytologic studies, this disease is still a great rarity. This is somewhat surprising in view of the abundance of smooth muscle found in the bronchial tree, existing as branching and anastamosing bands extending between the cartilages in the trachea and bronchi, and as very extensive converging bands of fibers at the carina.[1]

Neumann,[2] in 1938, mentioned two cases of leiomyosarcoma of the lung found at autopsy. He referred to an 83-year-old woman in whom the tumor was found at post-mortem examination. No information regarding the symptoms was given. The second case was that of a 66-year-old woman who had dyspnea, weakness, and weight loss. The patient died about one week later

and at autopsy a tumor of the left lung was found. The left upper lobe was atelectatic. Numerous metastatic nodules were found in the contralateral lung and the mediastinum, pleura, adrenal, thyroid, pancreas, liver, kidney, and bone.

Brunn and Goldman[3] in 1940 reported a case of polypoid tumor of the left lower lobe. A thoracotomy was advised, but the patient refused and he died five months later. A leiomyosarcoma was found in the left lung at autopsy. Randall and Blades,[4] in 1946, reported a primary bronchiogenic leiomyosarcoma in a 34-year-old Negro soldier. The initial diagnosis was made at bronchoscopy. The patient died before the tumor could be resected. A post-mortem examination revealed a mass at the right hilum extending into the upper lobe. More recently, in 1951, Freireich and associates[5] reported a case similar to ours in many respects. The principal difference is that the tumor in their case was covered by epithelium and was well encapsulated. It did not invade the bronchus. The diagnosis was bronchiogenic leiomyoma.

The extremely small incidence of pulmonary leiomyosarcoma should make one critical of the diagnosis. Benign tumors were discarded because of the invasion of the bronchial wall, the pleomorphism and the cellular reaction. Bronchial cancers were considered but the ovoid and fusiform cells in interweaving sinuous bundles and layers, suggest sarcomas. Neurofibrosarcoma and fibromyosarcoma were reviewed, but the pathology more nearly suited the leiomyosarcoma.

SUMMARY

1. A case of leiomyosarcoma of the lung is reported.

2. The patient was well and showed no signs of disease two years after resection.

3. It is believed that this is the third case of primary leiomyosarcoma of the lung on record, and the first to be treated successfully by pneumonectomy.

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GANGRENE FOLLOWING LUMBAR SYMPATHECTOMY FOR ARTERIOSCLEROTIC PERIPHERAL VASCULAR DISEASE

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THE occurrence of gangrene soon after lumbar sympathectomy for arteriosclerotic peripheral vascular disease has suggested to several observers that the sympathectomy itself had precipitated the gangrene. Popoff[1] suggested that the opening up of the arteriovenous anastomoses described by Hoyer and Sucquet shunted the arterial blood from the capillary system directly into the veins. Atlas,[2] in 1942, described three cases of gangrene following lumbar sympathectomy for advanced occlusive disease. He attributed the gangrene to the opening up of these arteriovenous communications. Freeman, Leeds, and Gardner[3] reported four cases of gangrene following lumbar sympathectomy which they thought attributable to the opening of numerous arteriovenous communications and the resultant deprivation of the nutrient capillary bed of arterial blood. They suggested that the operation may be contraindicated in advanced obliterative arterial disease in the absence of evidence of abnormal vasoconstriction or when vasomotor tone was low. These observers pointed out that this was a hypothetical explanation and lacked adequate proof. Felder and associates[4] have demonstrated significant drops in the skin temperature of extremities under ether anesthesia, and state that previously sympathectomized extremities are more susceptible to such drops in skin temperature during anesthesia. They state that on several occasions gangrene has been observed to develop in previously sympathectomized extremities immediately after a later operation performed under ether anesthesia.

In a wide experience we have seen but two cases of gangrene occurring immediately after lumbar sympathectomy for obliterative arterial disease. In the first case gangrene appeared in the toes on the third postoperative day and in the second case gangrene began five hours after the completion of surgery. In each instance an acute arterial thrombosis was the precipitating factor.

CASE REPORTS

CASE 1.*—S. J. (Charity Hospital of New Orleans, No. 43086), a 45-year-old Negro man was admitted June 27, 1946, with the chief complaint of coldness and itching of the right fifth toe of one year's duration. These complaints spread to involve the entire foot a few weeks prior to admission. No intermittent claudication had occurred. Examination showed coldness of the right foot with no pulsations below the popliteal surface. There was a mottled appearance to the plantar surface of the foot. Examination showed the left leg to be normal. A right lumbar sympathetic block was performed with relief of symptoms.

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*Mentioned in (1) Discussion by Dr. Alton Ochsner of paper by Freeman, Leeds, and Gardner,[3] and in (2) Paper by De Bakey, Creech, and Woodhall.[6]

The patient was thought to have degenerative vascular disease with a marked spastic element. On July 11, 1946, a right lumbar sympathectomy was performed under ethylene and ether anesthesia. The foot became warm and dry. Pulsations did not appear. On the third postoperative day the patient complained of pain across the dorsum of the right foot. The toes rapidly became gangrenous. On July 22, 1946, a right supracondylar amputation was performed. Examination of the blood vessels showed medial arteriosclerosis with thrombosis of a branch of the posterior tibial artery.

Under the stress of unilateral ambulation, symptoms rapidly appeared in the left leg. Left lumbar sympathectomy was performed on Sept. 19, 1946, under cyclopropane and spinal anesthesia, and on Nov. 27, 1946, left below-the-knee amputation was performed for developing gangrene of the left foot.

CASE 2.—J. H. (Macon Hospital No. 140147), a white man, aged 64 years, had had intermittent claudication in both calves for a period of three years. This had been of sufficient severity to cause him to lead a life of restricted activity. The complaint had become progressive, particularly on the right calf, despite this. Shortly before consultation he had fallen while walking, when both legs appeared to "give way." Past history and family history were noncontributory. Physical examinations revealed a short, stocky robust-appearing man. The positive physical findings were limited to the extremities. The femoral and popliteal pulsations were present and strong bilaterally. The dorsalis pedis and posterior tibialis pulsations were absent in each extremity. Both feet were cool; the right more than the left. On dependency, rubor appeared, and, on elevation, both feet appeared cadaveric with slow emptying and filling of the veins. Checkup examinations showed a marked variation in the warmth of the feet, and it was thought that vasospasm was marked. The usual laboratory examinations of the blood and urine were normal.

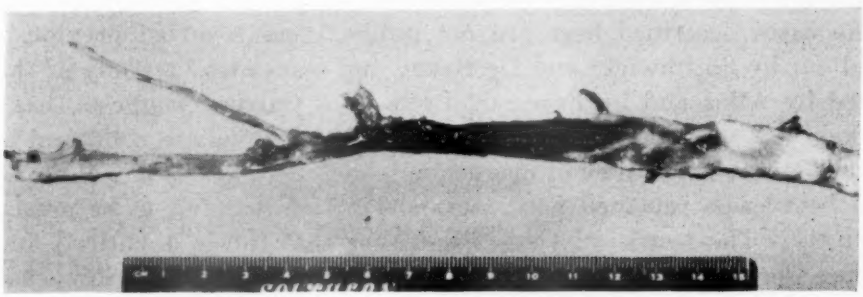

Fig. 1.

On Dec. 27, 1951, the patient was admitted to the hospital and a bilateral lumbar sympathectomy performed without incident. Spinal anesthesia, using 12 mg. of Pontocaine Hydrochloride, was employed. At about 4 P.M. on the day of surgery, when the patient was fully reacted and comfortable, he noticed the appearance of severe pain in the toes of the left foot. Pain and a feeling of numbness ascended the leg to below the knee during the succeeding hour. The foot and leg were cadaveric, cold, and excruciatingly painful to touch. Tenseness and swelling of the calf appeared early. This complication had its onset five hours after the completion of surgery. During the succeeding four days, while the patient refused ablation, various measures including fasciotomy were employed to relieve pain without avail. On Jan. 3, 1952, supracondylar amputation and common femoral vein ligation were performed.

On Jan. 15, 1952, the patient was discharged, primary healing of the stump having taken place. At home the patient rapidly became accustomed to his crutches and appeared to be making satisfactory recovery. On Jan. 22, 1952, nineteen days following amputation

and four hours after a physical checkup in his home, he died suddenly with symptoms suggestive more of a coronary thrombosis than of pulmonary embolism. No post-mortem examination was performed.

On dissection of the amputated leg, a firm clot was present in the lower popliteal artery and, in continuity, in the posterior tibial artery as demonstrated in Fig. 1. To gross examination there was no arteriosclerosis. Microscopic section showed a large artery with evidence of moderate intimal thickening. The surface layers were disrupted, showing subintimal hemorrhage and hemosiderin pigmentation. The attached thrombus demonstrated moderate layering of leukocytes and red cells. It was the opinion of the pathologist* that this represented a recent thrombus.

DISCUSSION

These two cases demonstrate rather dramatically one of the complications of arteriosclerotic peripheral vascular disease. It has long been our impression from pathologic examinations of limbs amputated for gangrene that the advanced degree of occlusion of the vessels, or the presence of a thrombus in one of them, was sufficient explanation for the gangrene. The addition of lumbar sympathectomy to the armamentarium of the vascular surgeon has confused the issue somewhat. We noticed previously that those patients who came to amputation after lumbar sympathectomy usually did so within four months after surgery, but the vast majority of these patients already had frank gangrene or impending gangrene. The extent of their disease before sympathectomy was sufficient reason for a poor result following sympathectomy, and any salvage which was considerable was all to the good and was but an additional reason for the application of this therapy to unselected cases.

The cases described here are not unlike those reported previously. As pointed out by Smithwick[5] and De Bakey and associates,[6] a study of the cases reported by Atlas and by Freeman, Leeds, and Gardner suggests that recent acute vascular occlusion had occurred and that inadequate collateral circulation was present at the time of operation.

In both cases reported here, vasoconstriction was felt to be present preoperatively. The course of Case 1 indicates that this was entirely incorrect and that the presence of extensive obliterative disease and low vasomotor tone was, in fact, the actual situation. In Case 2 extensive occlusive disease was not present and vasoconstriction was marked. The occurrence of this acute thrombosis is not readly explained. Before the thrombosis appeared, both feet and legs were warm and dry. The right foot, which had been painful preoperatively, felt comfortable to the patient. When the thrombosis occurred on the left, the patient was in the sitting position. Shortly after the thrombosis, the bleeding time was 30 seconds, coagulation time 5 minutes and 30 seconds, prothrombin time 23 seconds, 42 per cent. It was felt that this thrombosis had occurred without reason except that the position of the patient may have produced some stasis in blood flow. If the lumbar sympathectomy per se influenced this result, it would appear that arterial thrombosis and gangrene would be common immediately after lumbar sympathectomy, rather than as rare as it is.

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We feel that gangrene occurring immediately after lumbar sympathectomy is commonly the result of the extent of the disease process present at the time of sympathectomy or of the progression of vascular occlusion after sympathectomy. This may be sudden, as in arterial thrombosis of a major vessel, or more gradual, as the blood supply to the extremity is reduced by minor thromboses or occlusive arteriosclerosis. It is important, however, to recognize that other factors may occasionally operate to reduce the blood supply in the sympathectomized extremity.

White and Smithwick[7] have described a "sensitization to adrenalin" effect in sympathectomized extremities appearing on the third to fifth postoperative day and lasting for thirty-six to forty-eight hours in which sweating, color changes, and coolness of the extremity occur. Although we have recognized this to be present clinically from time to time, we have never thought the effect to be severe enough to cause gangrene or to contribute to the appearance of gangrene. The possibility that such cases could occur, however, remains.

Not dissimilar to the White-Smithwick reaction, except in time of appearance and possible causative factor, are the observations made by Felder and associates on unsympathectomized and sympathectomized limbs under ether anesthesia. We have not observed this effect under spinal or cyclopropane anesthesia, the types of anesthesia which we commonly employ. This adrenergic-cholinergic response of a sympathectomized limb to ether or local tissue anoxia produced by it requires an explanation compatible with the simultaneous production of adrenalin and a cholinergic substance acting in accord with Cannon's Law of Denervation. It is not known whether the reaction arises from the effect of tissue anoxia or its products upon the ganglia, or peripherally upon the smooth muscles of the arteries and upon the sweat glands.

The major difficulty of this observation is that if it is a result of tissue anoxia rather than the chemical ether itself, it should be a common observation and gangrene immediately following lumbar sympathectomy should be of frequent occurrence, which it definitely is not. One can hypothesize, of course, that an occasional patient will prove to be a hyper-reactor to the stress of surgery, permitting a greater release of adrenalin and cholinergic substances, or that an individual's nervous tissue becomes reactive to such chemical mediators to a greater degree than does that of others; then the rare occurrence of gangrene immediately after lumbar sympathectomy without arterial occlusion or thrombosis may be explained.

SUMMARY

Two cases of gangrene following lumbar sympathectomy but produced by arterial thrombosis are recorded. The theories presented for the explanation of gangrene following lumbar sympathectomy are discussed. It is suggested that factors other than vessel occlusion by disease or thrombosis may occasionally

influence the appearance of gangrene, but that the demonstration of such factors remains inconclusive as to their importance in producing gangrene after lumbar sympathectomy.

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Editorials

Parenteral Fluid Versus Parenteral Food

SINCE life is impossible for very long without water intake, it is not surprising that the term *parenteral fluid,* as first used, applied to the injection of simple solutions whose primary purpose was to provide water for patients unable to take anything through their gastrointestinal tract. By contrast, the objective of *parenteral food* is much wider, i.e., to provide all of the nutritional elements, not merely water alone. This objective can now be reached, but not without applying available specific knowledge. The surgeon can no longer be content with ordering a few liters of parenteral fluid without specifying whether it is to be 5 per cent glucose in saline or 10 per cent glucose with or without saline or amino acids (or leaving it to the discretion of the relatively untrained house staff). The exact amount of each of the various elements should be prescribed.

Fortunately, the daily maintenance needs for water, electrolyte, and vitamins can be fully met by injection without difficulty, because the amounts are so small, i.e., 2 L. of water, 3 to 4 Gm. of sodium and potassium chloride and phosphate, and up to a gram of the various vitamins for a normal-sized adult under basal conditions. However, the danger of giving too much, particularly of water and/or salt, must be avoided. Caloric and protein needs offer quite a different problem because these elements comprise over 95 per cent of the solid bulk of the normal diet. Actually even these needs could be fully met with 500 Gm. of glucose and 100 Gm. of an amino acid mixture. This would mean the infusion of 5 L. per day in order to avoid too hypertonic solutions. Because of the practical difficulties and the excessive water intake involved, such a regimen has not been used or even widely advocated. Most surgeons have been content to give a much smaller intake of 100 to 200 Gm. of glucose with or without amino acids in 2 or 3 L. of water, which is 75 to 50 per cent subcaloric.

In order to evaluate the physiologic significance of such a subcaloric intake, a clear distinction must be made as to whether or not protein food is also provided. If no protein is given, a full caloric complement of 500 Gm. of glucose is no better than the usual 100 to 200 Gm., because it has been shown that 100 Gm. of glucose are as effective as 200 Gm. in sparing body protein. Thus there is a definite limit to the usefulness of dextrose without protein.

When protein is given with an inadequate caloric intake, the situation is quite different, for under these circumstances it becomes important that one determine the degree to which the amino acids are used for energy rather than for tissue synthesis. Although a full caloric intake is necessary to achieve *maximum* protein utilization, it has been repeatedly shown by biochemists that protein is utilized even when the caloric intake is reduced. Perhaps the practical

difficulties of providing full calories will be largely overcome when intravenous fat becomes available. Intravenous alcohol has been successfully employed as an added source of calories, but somehow has not achieved very wide acceptance, possibly because of its side effects and possibly because its use is so intimately associated with social, psychologic, and even religious taboos. However, it is important to recognize that tissue protein synthesis does occur in protein-depleted patients who are given inadequate calories, provided they are simultaneously supplied with protein. For this reason it is of great practical importance to know the extent to which the daily protein needs can be met on inadequate caloric intakes.

Measurement of nitrogen balance is one way of answering this question. When nitrogen balance is zero, tissue protein is being neither lost nor gained; when nitrogen balance is positive, new protein tissue is being formed; when negative, protein tissue is being lost. There are degrees of positive balance as well as of negative nitrogen balance. While a positive nitrogen balance is highly desirable in that it means tissue protein synthesis, it must also be emphasized that, when this is not possible, a reduction in the degree of negative balance is beneficial because it reduces the amount of tissue protein wasted. The magnitude of negative nitrogen balance on a nonprotein intake is scarcely changed, as already noted, when the amount of glucose injected daily is increased from 100 to 200 Gm. or more. By contrast, a definite and often a pronounced reduction in the magnitude of negative nitrogen balance nearly always occurs when 100 Gm. of amino acid mixture are added to 100 Gm. of glucose. Indeed, such an intake is sometimes followed by a positive nitrogen balance, although the magnitude of its effect is determined by many factors, especially the amount of tissue protein previously lost and not solely by the energy needs. That protein can be utilized in spite of inadequate calories has also been established in other observations with oral feeding as well. This phenomenon is of practical importance because it means that during critical periods when a full caloric intake is temporarily impossible or undesirable, tissue protein wastage can still be reduced or prevented. A mixture of protein and carbohydrate is better nutritionally than carbohydrate alone, even when calories are inadequate. In terms of parenteral nutrition limited to 200 Gm. of solids in 2 L. of water, it is, therefore, preferable to give 100 Gm. each of an amino acid mixture and glucose, than 200 Gm. of glucose alone. A patient should not be deprived of all protein food just because it is not feasible to achieve the most efficient utilization thereof:

"Half a loaf is better than none."

—*Robert Elman*

Mitral Stenosis: The Surgeon's Role

WITH any grave lesion, the need of supplementing nonoperative management by surgical techniques will inevitably produce doubts and mental reservations as well as gratifying moments. To adopt the wisest course for each case assuredly requires both an open mind and an attitude of most careful inquiry on the part of all physicians concerned. This transition time in our thinking exists now in regard to surgical therapy for rheumatic valvular heart disease. Just as the inherent challenge in medicine is to restore health, an equal obligation exists to do no wrong to the patient. When faced with these alternatives, one surgeon may unhesitatingly choose to operate; another will be willing to proceed only after the most careful and detailed study possible for each patient, both before and in the weeks succeeding an operation. For any physician to look upon each instance of mitral stenosis as an immediate surgical challenge would represent as pathetic a disservice to medicine as would exercising surgical management only for all individuals suffering from a duodenal ulcer.

True, we need no longer question the feasibility of surgical treatment for certain cases of mitral stenosis. The technique of mitral valvuloplasty has been tested, and for the proper case will largely correct, for the time being, the stenotic lesion, with demonstrable attendant benefits to the patient in increased physical activity. The question alarming many deeply interested in this disease is: Has technique surpassed knowledge? Merely being able to perform an operation should not justify the performing of it. Assuredly there are cardiac states for which an operation is regularly required—for example, patent ductus arteriosus. Proof is yet lacking, however, that one should operate upon all cases diagnosed as mitral stenosis. The accumulation of a large operative series is but one way to settle this question. At least as acceptable an alternative is an attempt at careful clinical evaluations and precision measurements which seek to chart the physical changes taking place as a consequence of the disease and the alternation of these values after surgical treatment.

Approximately two out of every three severely symptomatic patients who undergo surgery can expect marked relief from the operation. In order neither to deny the operation to those who might be benefited by it nor to urge it unnecessarily, it is highly essential that we improve our discrimination techniques. It is at the extremes of this disease complex, with our patient either very sick or very healthy, that one can most easily err. In brief, there can be little quarrel with the selection of surgery for a young adult gradually succumbing to a lingering illness, relatively uncontrollable by all the variants of medical management. There is, however, a reasonable reluctance on the part of many clinicians to be persuaded that the diagnosis of mitral heart disease should invariably lead to a cardiotomy for exploration as to the type and degree of heart disease, as some surgeons have seriously suggested. This hesitancy is compounded in part from a recognition that with the most favorable clinical results, and in the experience of many surgeons, there is yet present, upon auscultating these patients postopera-

tively, the pathognomonic cardiac rumblings of mitral heart disease. In addition, our medical associates are deterred by the fact that most sufferers with mitral stenosis know of their heart disease and hence are often earnestly desirous of realizing some improvement from this operation. In this group, to depend on a purely subjective analysis of alleged benefits is to abandon science for hearsay. Our future progress and the patient's best interests rather seem to lie in the direction of expanding clinical and physiologic techniques so that a more reliable appraisal before and after surgery may become possible. A careful and sustained follow-up of these measurements, particularly where there is any apparent regression of benefits, may be invaluable in the chronicling of data from which all of us can derive guidance.

—*Richard L. Varco*

Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

RHABDOMYOSARCOMA OF SKELETAL MUSCLE

REPORT OF 100 CASES

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CLINICAL STUDY OF SARCOMA OF STRIATED SKELETAL MUSCLE

IN THE 20 year period from 1929 to 1949, 100 cases of striated muscle sarcoma have been seen on the ward and private services at the Memorial Cancer Center. In each instance there has been histologic verification of the diagnosis. In the vast majority of cases the diagnosis was made on the basis of a section from the operative or biopsy specimens at the Memorial Hospital. In a few cases in which the tumor was biopsied or operated upon elsewhere and then referred for additional treatment, the original slide or paraffin block was obtained and reviewed by the pathology department at the Memorial Hospital. Rhabdomyosarcomas occurring in the head and neck are not included in this series. The statistical data reviewed in this study are based solely on the tumors of skeletal muscle, because it is our opinion that the inclusion of visceral, lingual, and cardiac muscle tumors confuses the conclusions drawn about methods and end results of treatment. Our experience naturally includes the myogenic tumors of divers types which will be summarized briefly and illustrated by case reports.

HISTORICAL NOTE

Tumors of striated muscle have been recognized since 1854 when C. O. Weber, writing in *Virchows Archives,* described a tumor in the tongue of a 21-year-old man. The tumor was surgically excised but recurred. On histologic examination the tumor was found to be composed of striated muscle cells showing all stages in development from embryonal to adult cellular structures. Other ancient case reports in the literature, not all of which are verified, were by Billroth (1856), Buhl—2 cases (1865), Ribbert—2 cases (1891), Bayer—orbit of child (1882). Since these early descriptions there have been many publications dealing with the embryology and histology of these tumors. Their occurrence has been described in fish, birds, rats, and mice. In 1943 Nettleship,[28] in the *Journal of the National Cancer Institute,* described a spontaneous, transplantable, mature type of rhabdomyosarcoma in Strain C mice. This tumor was similar to such tumors in man, but contained more adult type of cells with intact cross striations and myofibrils. In earlier years, arguments

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waged that true muscle tumors did not occur and that such neoplasms actually originated from the connective tissue septa within the muscle bundles, but now with selective staining and more exact histologic criteria, there is, of course, incontestable proof that rhabdomyogenic tumors do exist. The experience of any one physician or institution with this rare neoplasm has been so limited that little is known about its natural history or behavior and certainly this knowledge cannot be accurately gleaned by summarizing case reports culled from the literature in lieu of personal experience.

Fig. 1.—Fungating congenital rhabdomyosarcoma of the lower leg. Surgical dissection with preservation of the leg.

NOMENCLATURE OF STRIATED MUSCLE TUMORS

The chance location of the tumor within the muscle bundles and even invasion of muscles by the sarcoma has led to the improper inclusion of a large group of tumors under the classification of sarcomas of the skeletal muscles. The title under these circumstances is a misnomer as it refers only to the location of the tumor within the muscle and not to its histogenesis, on which the proper nomenclature should be based.

Rakov[34] prefers the term "malignant rhabdomyoblastoma" because it applies to tumors consisting of immature striated muscle cells which show infiltrative destructive growth and a capacity to metastasize. He has rejected the terms "myosarcoma" and "rhabdomyosarcoma" as unsuitable, because they imply incorrectly an origin from mature striated muscle cells. Our conception of the usage of these various terms is adumbrated in the accompanying classification.

CLASSIFICATION OF TUMORS OF STRIATED MUSCLE

No classification of these tumors can be made which will satisfy all people and which will clarify all objections. The student of muscle tumors is indebted to Abrikossoff,[1, 2] Cappell and Montgomery,[9] and especially to Arthur Purdy Stout for contributions elucidating the various categories. In our opinion, a clinical as well as a histologic grouping is necessary for the understanding of the neoplasms and therefore the following outline is submitted.

A. *Nonmyoblastic Tumors Involving Skeletal Muscles.*—These are of clinical interest because of the difficulties of differential diagnosis and the similarity of indications and plans for treatment.

1. Sarcomas originating within the gross muscle bundles from connective tissue or stromal elements such as the perimysium, the interfascicular connective tissue and the perineural or perivascular connective tissue. Sarcomas developing in myositis ossificans would be a classical example.

2. Sarcomas developing without the muscle but invading it secondarily and by continuity, for example, parosteal bone sarcomas, fibrosarcomas and malignant neurilemmomas.

3. Sarcomas metastatic to muscles from distant sites, for example, synoviomas and liposarcomas.

B. *True Myoblastic Tumors of Skeletal and Other Striated Muscles.*—The striated muscle cell is certainly not a common component of tumors, considering the vast number of neoplasms which occur in human beings, but it is found in full or complete differentiation in the following instances:

1. Teratomas and mixed-cell tumors of various organs such as the testis, kidney, ovary, and prostate. Some of the best opportunities to study the well-differentiated striated muscle tumor cell are in this moiety of the malignant mixed tumors, examples of which are the sarcoma botryoides of the uterovaginal canal and the Wilms' embryonal adenomyosarcoma of the kidney.

2. Congenital myoblastomas of the tongue and of the cardiac muscle. These latter muscle tumors and neoplastic-like tumefactions of the heart are sometimes associated with other abnormalities such as tuberous sclerosis.

3. Malignant myoblastic tumors of skeletal muscle. These neoplasms comprise the body of this report and constitute the only group involved in the statistical analyses. Abrikossoff,[2] in 1926, and later in 1931,[3] subdivided these neoplasms of skeletal muscle into 4 histologic groups, which are probably not different types, but represent degrees of differentiation of these

tumors. He described the round, oval, or elongated mononuclear cells, 20 to 26 μ long, occurring in bundles, possessing granular acidophilic cytoplasm, and with or without longitudinal or cross striations.

a. Pure myoblastoma—composed of myoblasts without striations. These cells morphologically and tinctorially resemble skeletal muscle cells.
b. Myoblastoma—with similar cells except that longitudinal or cross striations or both may be found imperfectly developed in the periphery of the tumor cell.
c. Rhabdomyosarcoma—with hypertrophic myoblasts, some enormous (40 to 150 μ long), frequently multinucleated and syncytial, with occasional striations.
d. Rhabdomyosarcoma—with atypical myoblasts, anaplastic, polymorphic-celled, with regions of high differentiation showing longitudinal and cross striations.

INCIDENCE OF RHABDOMYOSARCOMA

Considering the enormous amount of voluntary muscle which comprises the human body, the incidence of muscle tumors is amazingly low. On the basis of relative weights per pound of human flesh, skeletal muscle has fewer tumors than any other tissue. There is practically no information in medical literature concerning the incidence of this tumor, but it must be a very rare neoplasm. The rarity of rhabdomyosarcomas must be due to the fact that striated muscle cells are completely differentiated, and do not undergo cellular division in postnatal life as do the cells in skin, bone, breast, and the mucosae.

At the Oncological Institute in Leningrad,[34] 20 per cent (17 cases) of the sarcomas of soft somatic tissues treated between the years 1926 to 1934 were rhabdomyosarcomas. The 100 striated muscle sarcomas comprising our report represented 13.9 per cent of our 717 sarcomas of soft somatic tissues, so it is a rare histogenetic type in a scarce group of malignant tumors (Table I).

TABLE I. MALIGNANT TUMORS OF THE SOFT SOMATIC TISSUES; DISTRIBUTION ACCORDING TO HISTOLOGIC TYPE

HISTOLOGIC TYPE OF TUMOR	NUMBER	PER CENT
Sarcoma of undetermined histogenesis	261	36.4
Liposarcoma	105	14.6
Rhabdomyosarcoma	100	13.9
Synovioma	60	8.4
Kaposi's sarcoma	48	6.7
Malignant neurilemmoma	46	6.4
Fibrosarcoma	39	5.4
Dermatofibrosarcoma Protuberans	39	5.4
Angiosarcoma	19	2.6
Total cases	717	100.0

AGE AND SEX DISTRIBUTION

For some unexplained reason, the rhabdomyosarcomas occur with somewhat greater frequency in men, for example, 61 men and 39 women (Pack and Eberhart), 62 men and 52 women (Stout).

Rhabdomyosarcomas occur at all ages from early infancy to extreme old age. This tumor was found predominantly in middle and older age groups with 65 per cent in the 40 to 70 year age bracket and the highest incidence in the sixth decade (28 per cent). Our oldest patient was 78 years old and the youngest was only 5 weeks old. Moulonguet and Pollosson[26] have commented on a supposed relative immunity of children to this tumor; however, 4 patients in our report, of whom one has been cured for 13 years, were under 10 years of age. Since this statistical analysis was completed, 2 more children of 5 years of age had radical local dissections of rhabdomyosarcomas of the extremities.

TABLE II. RHABDOMYOSARCOMA OF SKELETAL MUSCLES; AGE OF PATIENTS

	ALL CASES THROUGH 1948		DETERMINATE CASES THROUGH 1943		FIVE-YEAR CURES THROUGH 1943	
AGE OF PATIENT	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
10 years and less	4	4.0	2	3.1	1	4.5
11 to 20 years	2	2.0	2	3.1	2	9.1
21 to 30 years	8	8.0	5	7.7	3	13.6
31 to 40 years	9	9.0	5	7.7	4	18.2
41 to 50 years	20	20.0	14	21.5	2	9.1
51 to 60 years	28	28.0	20	30.8	7	31.8
61 to 70 years	20	20.0	10	15.4	3	13.6
71 years and over	9	9.0	7	10.7	0	0.0
Total Cases	100	100.0	65	100.0	22	100.0

CASE 1. Congenital Rhabdomyosarcoma of Thigh (Thirteen-year Cure).—G. McC., a male infant, had a small lump on the anterolateral aspect of the left thigh which developed shortly after birth and grew slowly. When he was 2 months of age, the mother became sufficiently apprehensive to seek medical consultation. A radical surgical excision of the mass with the surrounding fascia and muscle was made. The tumor was a fibrosarcoma, grade III, with some foci strongly resembling rhabdomyosarcoma.

A bivalved body cast was applied with a fenestrated opening overlying the thigh in order to immobilize the infant while x-ray treatment was administered. High voltage x-ray therapy was given, using the following factors: 200,000 volts, 50 cm. target-skin distance, 0.5 mm. copper filter, field 9 by 8 cm., 25 Ma., 150 r. daily, a total dose of 2,400 r., dose to center of femur 2,280 r. The treatment was consummated in April, 1938.

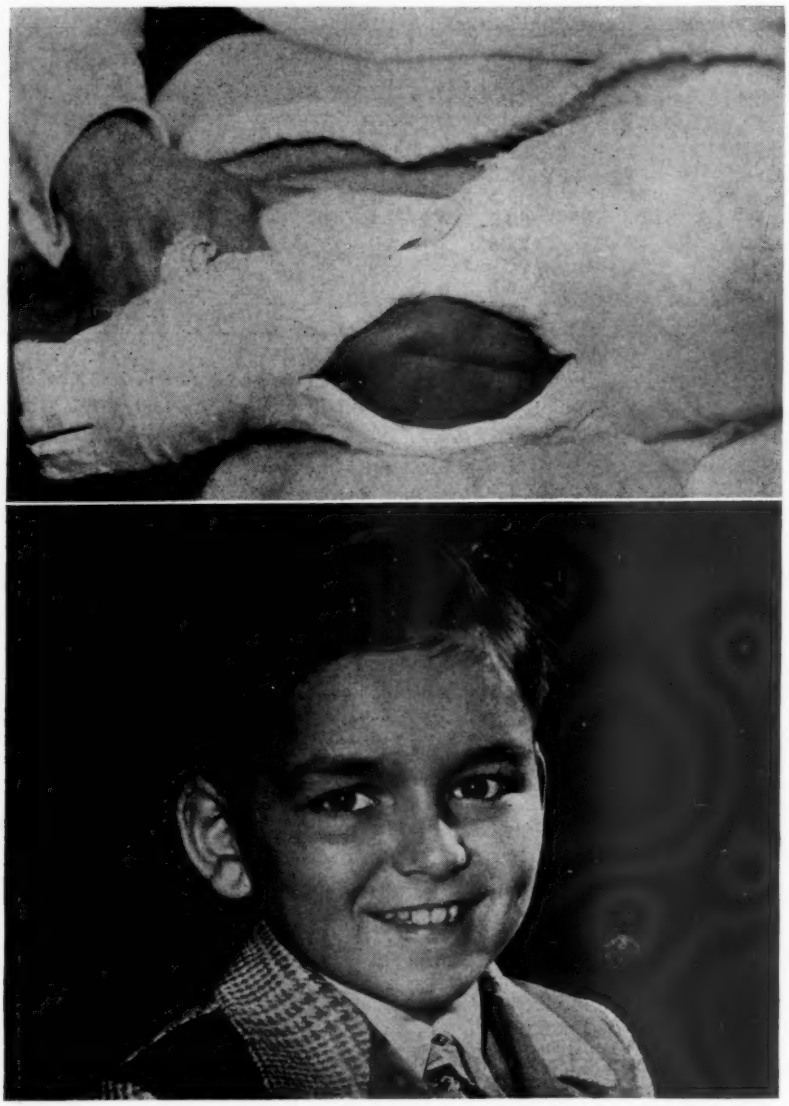
The child is now living and well without shortening of the extremity, without crippling deformity, and without recurrence, and is 13 years of age.

ETIOLOGICAL RELATIONSHIPS

The malignant tumors of striated muscle, or rhabdomyosarcomas, may originate from pre-existing benign myomas, but in the majority of instances seem to develop de novo. There is paucity of theories to explain the genesis of this tumor and none of them appear tenable except perhaps the theory that they are congenital. The striated muscle cell is a completely differentiated end product and according to embryologists is capable of enlargement but not of cell division in postnatal life. The repair of muscle is by fibrous tissue replacement and not by regrowth of new muscle cells. Furthermore, the best opportunity to study striated muscle neoplasia is the myogenic compound of teratomas and mixed-cell tumors, admittedly of congenital origin. There is no evidence to indicate that postnatal influences contribute to the genesis of rhabdomyosarcomas.

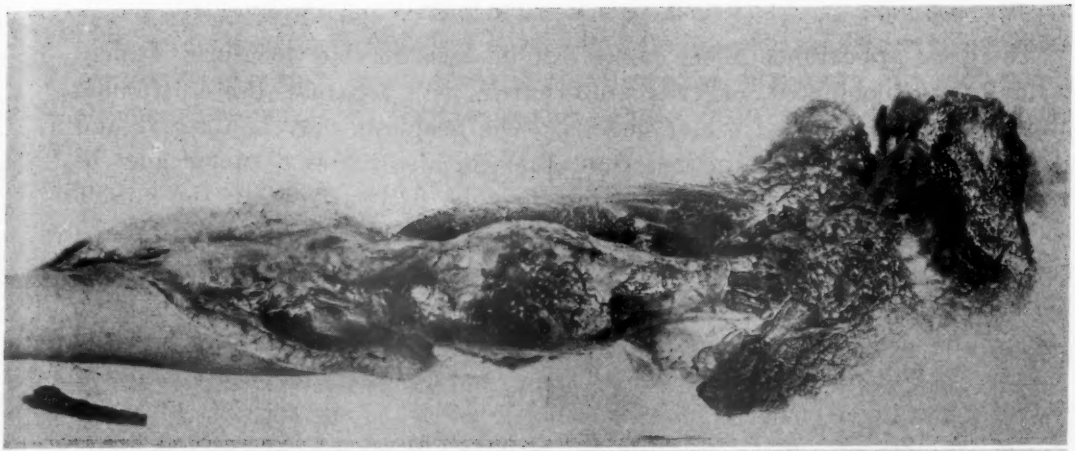
Trauma plays no role in the causation of these rhabdomyosarcomas but the limb or part containing the tumor is more predisposed to injury; in fact, treatment has often been delayed due to a presumptive and incorrect diagnosis of "charleyhorse." Seven patients were able to recall some type of trauma to the approximate location in the body where a muscle tumor subsequently developed. When we consider the number of bruised arms and shins which fall to the lot of the average individual it seems safe to disregard trauma as an etiological factor.

A.



B.

Fig. 2 (Case 1).—*A*, Congenital rhabdomyosarcoma of the thigh. Newborn infant treated by surgical excision and postoperative x-ray therapy. X-ray treatment administered through window of immobilizing cast. *B*, Patient at the age of 12 years.



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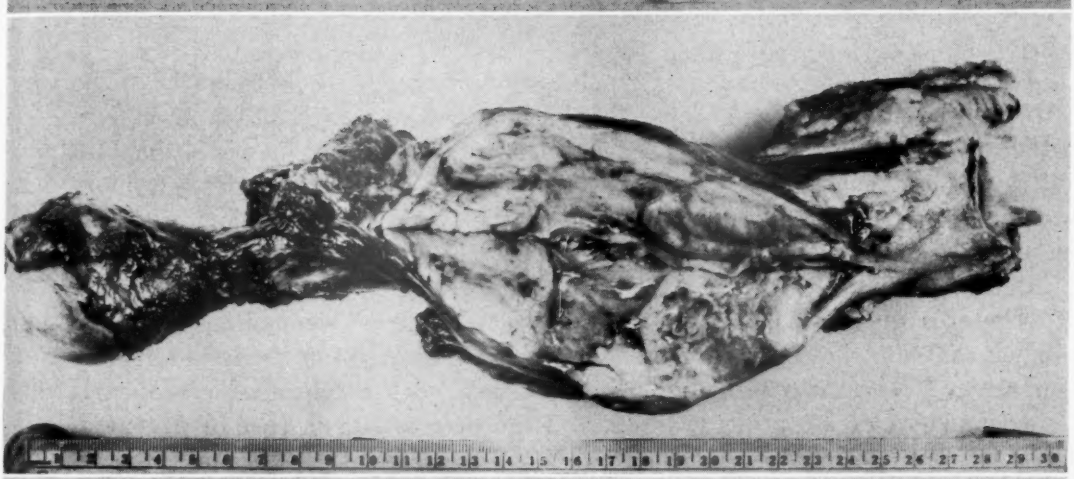

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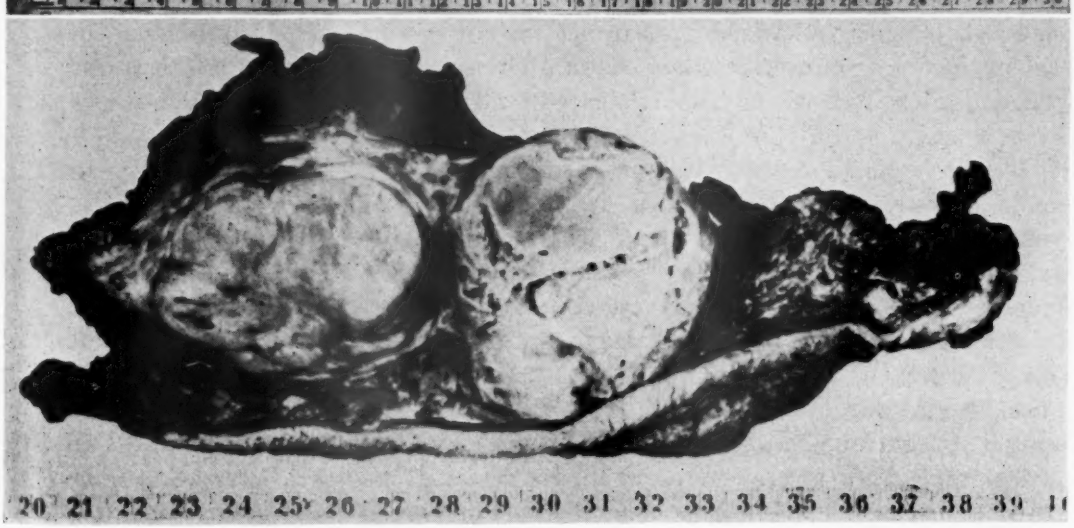


Fig. 5.

Fig. 3.—Rhabdomyosarcoma of the biceps muscle. The level of amputation is above the origin of the involved muscle.

Fig. 4.—Dissected gross specimen of rhabdomyosarcoma (amputation). Note smooth homogeneous structure seen on cross section with small intratumoral hemorrhages.

Fig. 5.—Multilobular tumor, showing pseudoencapsulation.

GROSS PATHOLOGIC ANATOMY

The gross appearance of the tumor exhibits considerable variation. It may be single, multilobulated, or even multicentric with separate discrete tumors comprising the pattern of tumor genesis. The neoplasm may be discrete and encapsulated or so diffuse in its extent that its identity as a tumor may be questionable at first. The tumor nodule may be flattened within the muscle sheaths. Although in gross appearance the tumors appear to be encapsulated or infiltrating, it would be better to consider the tumor as circumscribed rather than encapsulated, because, in truth, the appearance of encapsulation is an illusion; the neoplasm does extend far beyond the edge of the circumscribed growth. The disparate appearance of these 2 types is due to the manner of growth of the lesion, namely, by expansion in which the appearance of circumscription follows or by infiltration which is characteristic of the diffuse manner of growth.

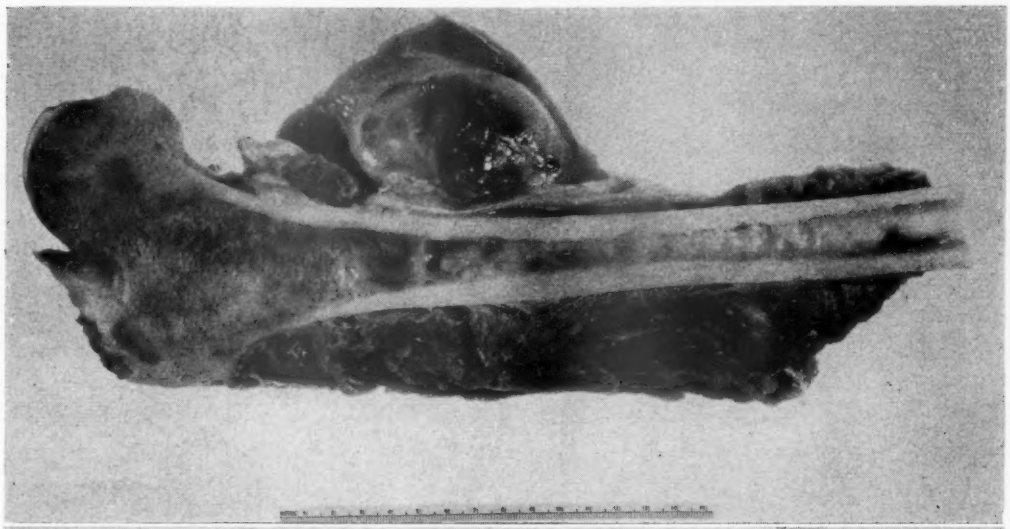
Gordon-Taylor[16] has stated this point of view succinctly as follows: "The distinction between the two groups is perhaps of academic rather than of clinical or therapeutic value, nor should the pathological anatomical classification into infiltrating and encapsulated forms be labored too zealously, for these tumors have no true capsule and the abolition of the word, encapsulation, is better calculated to relegate the operation of so-called enucleation for these tumors in the background."

There is great variation in the degree of hardness depending upon the collagen content; the connective tissue component of these tumors differs greatly in quantity. The softness also depends, in part, on the degree of vascularity, the existence of myxomatous changes, and the presence or absence of degeneration with cystic formation. Sometimes the tumor is quite soft and presents a mottled, grayish-yellow-red appearance on cut section. The lobulations appear outlined by connective tissue septa. Cystic cavitation may be the result of degeneration, necrosis or hemorrhage with absorption. Hemorrhagic necrosis may be massive and give the lesion the appearance of a large hematoma.

Hemorrhagic Rhabdomyosarcoma.—Extensive intratumoral hemorrhage can and does occur within the soft tissue sarcomas, more commonly in the rhabdomyosarcoma. The hemorrhagic necrosis is so massive that it resembles in this way the peculiarity of telangiectatic osteogenic sarcoma (the so-called malignant bone aneurysm). There is an extensive fluidlike spread along the fascial planes. The lesion bears a clinical resemblance to a large hematoma. When the fluctuant mass is sectioned, a gush of fluid blood occurs with extrusion of tumor substance, leaving large cavities lined by fibrin and occasional tumor tissue. The quantity of intramural hemorrhage contributes to a marked anemia. Two surgical difficulties are encountered in the removal of such a tumor: (1) the hazard of excision without rupturing the tumor and causing spillage into the operative wound; and (2) the amputation or dissection must be well above the superior limit of extravasated tumor tissue along the fascial planes. The prognosis is grave under these circumstances because of the frequency of pulmonary metastasis.

Multicentric Origin.—The multiplicity of these tumor nodules, each discrete and separate, has not yet been generally appreciated by pathologists and surgeons. We have encountered identical smaller tumors in adjacent muscle, although preoperatively only the major lesion was detected. This has led us to

Fig. 6.



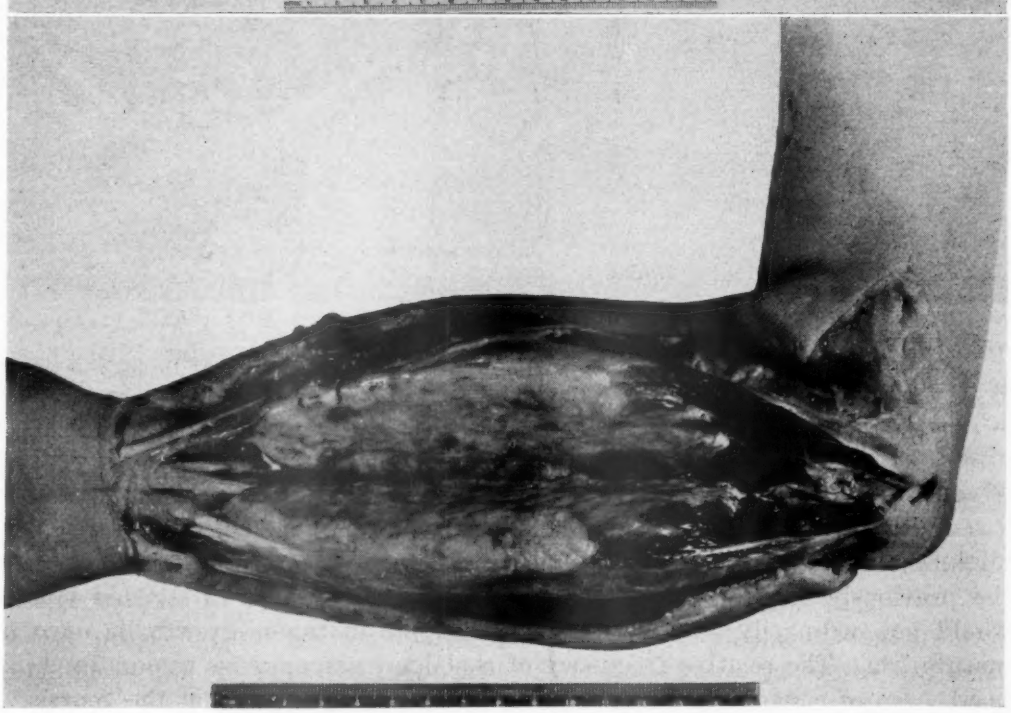
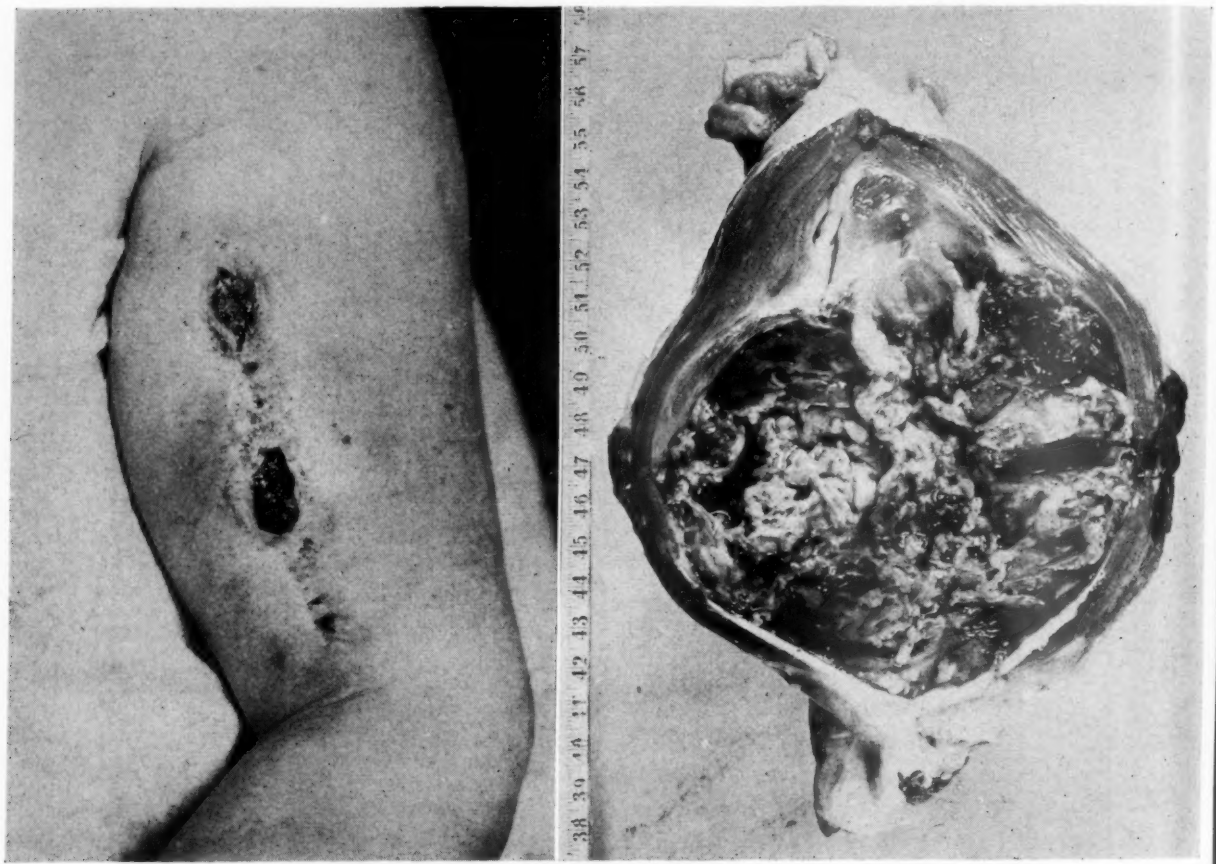


Fig. 7.

Fig. 6.—Rhabdomyosarcoma of the thigh. A second focus was found on the opposite side of the thigh. Segmental resection of the lung was performed four years later for two metastatic foci.

Fig. 7.—Rhabdomyosarcoma of the forearm. Dissected specimen to illustrate a common relationship of the tumor to muscle groups and tendons.

conclude that the rhabdomyosarcoma is occasionally multicentric in origin and offers the logical reason why the radical dissection should include a removal of the entire muscle in which the tumor develops and even the group of muscles, if more than one are involved by the multicentric tumor process.



A. *B.*

Fig. 8.—*A*, Rhabdomyosarcoma of the arm, recurrent and fungating through previous incision.

B, Gross specimen of rhabdomyosarcoma to show hemorrhagic necrosis and liquefaction in recurrent tumor.

EMBRYOLOGIC RELATIONSHIP OF STRIATED MUSCLE TUMORS

Keith[21] has declared that no new fibers are formed in skeletal muscles after birth, the growth of muscles in bulk being effected solely by enlargement of the previously existing cells. Tissue so well differentiated as striated muscle would not ordinarily be expected to participate in tumor growth de novo in mature life. The relative frequency of rhabdomyosarcomatous tumors in childhood, even of congenital origin, lends support to the theory that the genesis of many striated muscle tumors may be from prenatal life. Tumors composed of muscle fibers as the chief component may originate in the known groups of striated muscles or in remote regions wherein they are perhaps embryonal misplants.

Geschickter[15] summarized the development of muscle tissue as follows: "Within the first month of embryonic life, the mesoderm spreads out from the hind end of the embryo and separates into a paraxial mass, an intermediate cell mass and sheets applied to the body wall and primitive digestive tube. In the paraxial mesoderm and in the primitive body wall, the segmental voluntary muscles are developed. In the intermediate cell mass, the musculature connected with the urogenital organs develops and in association with the splanchnopleure, applied to the primitive gut, the muscles of the digestive tube the heart and the large blood vessels develop."

Cappell and Montgomery[9] have described the pattern of histologic evolution of the striated muscle cells as follows: "In its development, the voluntary muscle passes from a syncytial stage in the mesenchyme to a myoblastic stage and subsequently to a myofibrillar stage in which the developing muscle fibers show a beading effect followed by the appearance of cross striations. The primitive muscle cells or myoblasts are at first round and oval but rapidly become spindle-shaped while at first retaining their mononuclear structure. The spindle cells later elongate and their nuclei show mitotic divisions without separation of the cytoplasm, so that by the second month of embryonic life, multinucleated syncytial strands are formed, in the peripheral zone of which longitudinal fibrils appear while at the same time, the central zone remains undifferentiated and contains the nuclei of the muscle fiber. Later, as the fibrillation spreads to the center of the cell, the nuclei then migrate to the outer cytoplasmic layer, where they arrange themselves around a zone of clear sarcoplasm, from which the sarcolemma is later derived. They find that transverse striations appear only later after the fibrillation is well advanced."

HISTOPATHOLOGIC FEATURES OF RHABDOMYOSARCOMA

The rhabdomyosarcoma is such an infrequent tumor that few pathologists have been privileged to study the microscopic peculiarities of the neoplasm. It is very likely true that many sarcomas of this histogenesis have never been so labeled because the anaplasia on the one hand or the preponderance of fibroblastic tissue on the other, has influenced the examiner from labeling the histogenesis as of striated muscle origin.

Opportunity to study the rhabdomyosarcoma has been afforded by Nettleship's discovery of a spontaneous, transplantable, mature type of rhabdomyosarcoma of Strain C mice. The Nettleship tumor is histologically similar to such tumors in man and in domesticated animals, but contains more adult type of cells with intact cross striations and myofibrillae.

A promising aid for the microscopic detection of rhabdomyosarcomas has been the study of tissue cultures made from the human tumor in which the muscle cells are more readily identified. This important technique, developed by Margaret Murray and Arthur Purdy Stout,[27] stems from earlier tissue culture studies performed by Irene Pogogeff and Margaret Murray[32] in which skeletal muscle tissues of the adult rat were grown in vitro. They were able to observe muscle fibers on the fourteenth to fifteenth day of the culture. On the

sixteenth day they observed the fibers contract spontaneously and on the eighteenth day of tissue culture with the fibers still contracting, cross striations were observed. The application of this method of diagnosis to the analysis and study of human tumors of questionable muscle origin is most promising.

Normal skeletal muscle of vertebrates exhibits a constant and characteristic histologic pattern. The cross striations of human skeletal muscle fibers are striking and are associated with less conspicuous, lighter and darker linear fibrils running at right angles along the length of the fiber. The sarcomere is defined as the division of the fibril between 2 cross lines and the fibrils are designated as sarcostyles. It has been suggested that the beading of the sarcostyles is due to the distention of the sarcostyle during muscular contraction which causes it to bulge out between the discs. The nuclei of striated muscle are

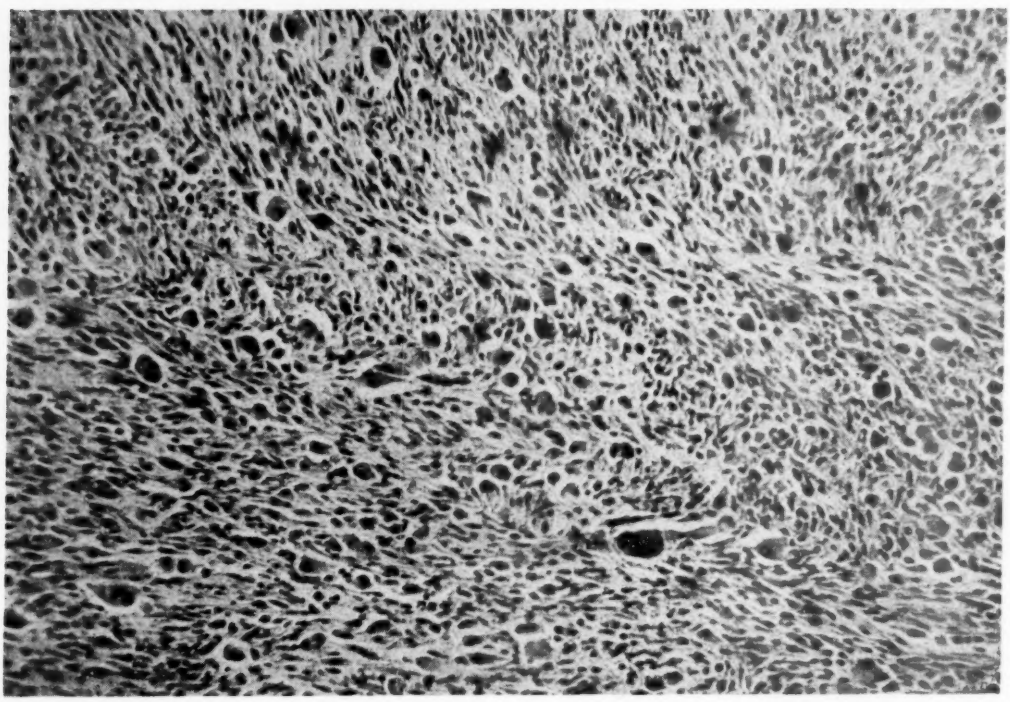


Fig. 9.—Rhabdomyosarcoma of the skeletal muscle. Distribution of the neoplastic muscle cells in fasciculi.

distributed irregularly along the fibers and immediately beneath the sarcolemma. The nuclei are about 10 μ in length and 5 μ in transverse diameter. The capillary blood vessels in normal muscle are numerous, but course in the interfibrillary spaces without entering the fibers. The skeletal muscle is invested by a coarse sheath surrounding the entire muscle bundle from which partitioning membranes are bundled into various sizes and ultimately form more delicate subdivisions between the individual muscles and fibers. The connective tissue component of the rhabdomyosarcomas varies greatly in proportion to the amount of tumor present and possibly modifies the rate of growth and course of the disease.

The diagnostic and microscopic features of rhabdomyosarcoma have been summarized by Rakov as follows: (1) A pronounced polymorphism of the tumor cells. (2) The presence of spindle cells. (3) The presence of giant cells. (4) The peculiar arrangement of the stroma. (5) The presence of fibrils which are sometimes cross-striated.

No one description of the microscopic picture of rhabdomyosarcomas can suffice because in certain instances the tumor may duplicate in structure the spindle-cell sarcoma of smooth muscle and in other instances, though within the same tumor, exhibit a multinucleated myoblastic stage in which the cells are large, elongated, and multinucleated. This feature of the rhabdomyosarcoma in which all phases of the histogenesis of the tumor are shown from areas of small spindle cells evidently representing the mesenchymal condensation, from which the early muscle tissue originates, to the more differentiated portion of the tumor which may exhibit both the cross and longitudinal striations. As far as possible the term rhabdomyosarcomas is used to denote those tumors arising in striated muscle and which are made up of cells possessing the characteristics that are generally accepted as those of rhabdomyoblasts.

Tumors of myoblastic origin may be identified in the absence of definitely cross-striated cells by the presence of centriole clusters and abortive fibril formation, according to Wolbach.[44] Arthur Purdy Stout has done much to clarify our knowledge about the histogenesis of this tumor and we therefore present his classification of the cell types. The rhabodmyoblastic tumor cell appears in three forms, in each of which the cytoplasm is eosinophilic and often granular: (A) The rounded-cell type, (B) the strap-shaped cell with 2 or more nuclei arranged in tandem formation, and (C) the racquet-shaped cell with a single nucleus at one expanded, rounded end, and a tapering body. Using either Heidenhain's hematoxylin or Masson's trichrome stain containing acid fuchsin, or phosphotungstic acid—hematoxylin with Zenker's fixation, Stout has usually been able to distinguish either the cross striations or the longitudinal myofibrils in the cells of these tumors.

The predominant cells of the rhabdomyosarcoma are long, spindle-shaped, relatively large (up to 100 μ) cells with homogenous or granular acidophilic cytoplasm. The nucleus is situated either in the center of the cell or is unipolar under which circumstance the cell tends to assume a racquet shape. The nuclei have been described as bean shaped by Rakov and the tandem arrangement of these bean-shaped nuclei produces the strap-shaped cell described by Stout. The cells may bifurcate at the end and form syncytial arrangements with many nuclei. Rakov believes that fibrils are most frequently seen in these syncytial masses. Vacuolization is occasionally seen in the peripheral cytoplasm. Mitoses are not commonly seen in the microscopic field.

Other types of cells are scattered among the spindle-cell elements. These include a small round cell with a dark compact nucleus and narrow rim of cytoplasm and a large polygonal cell with a pale vesicular nucleus. In all the rhabdomyosarcomas studied by Rakov at the Oncological Institute in Leningrad, he found giant cells of some type and he regards their presence as an

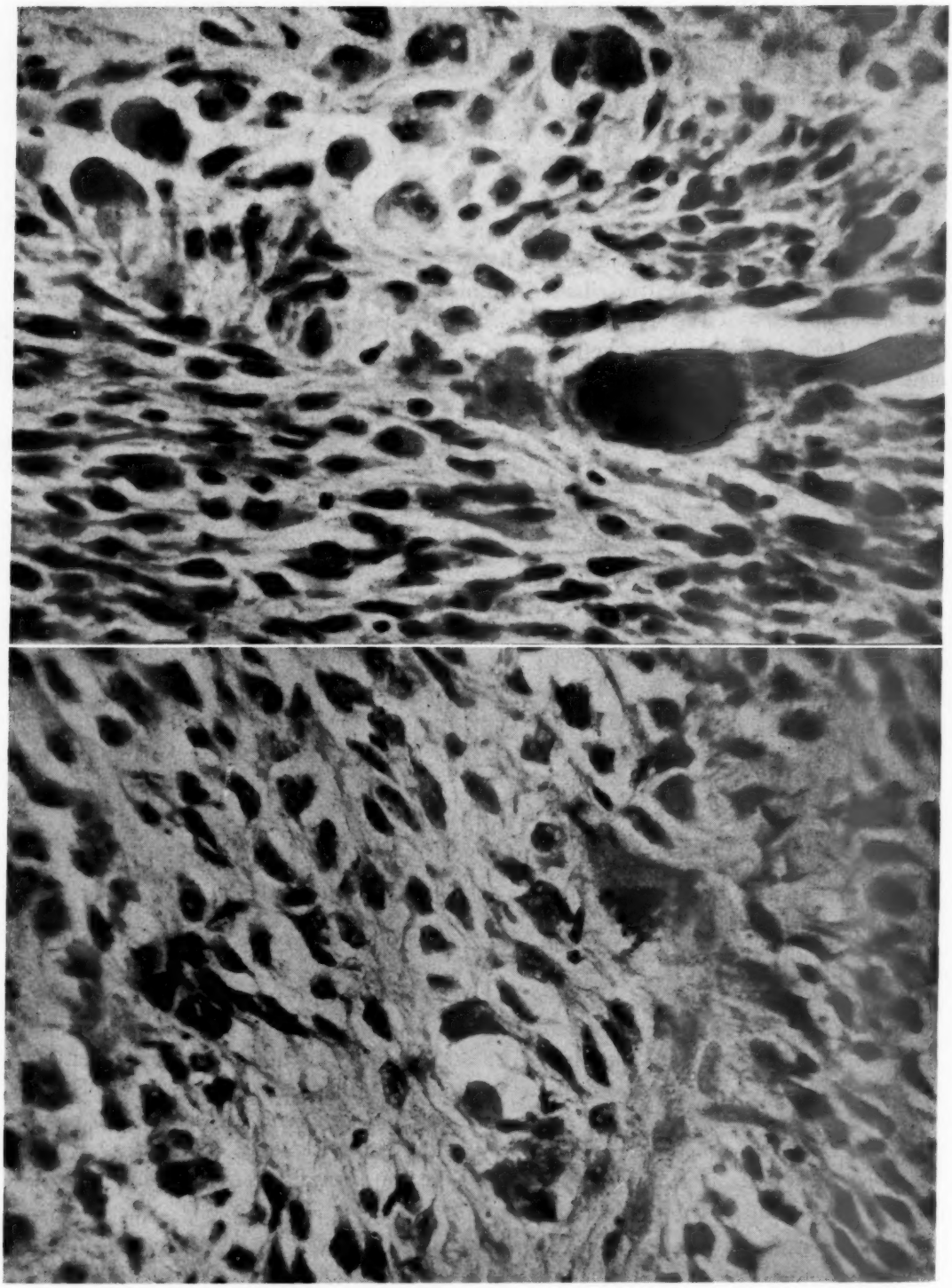


Fig. 10.—Rhabdomyosarcoma of the skeletal muscle, exhibiting giant, racquet, and ribbon cells characteristic of the tumor.

indispensable diagnostic feature of rhabdomyosarcomas. He divides the types of giant cells occurring in rhabdomyosarcomas into 3 groups: (1) The ordinary tumor giant cell 30 to 60 μ in diameter with a single bean-shaped nucleus and finely granular cytoplasm. (2) The large spindle-shaped cells measuring 150 to 200 μ in length. (3) The plasmodial-like cell, which is a rare type of giant cell consisting of an enormous oval or round structure covering more than a single high-power microscopic field and containing 10 or more nuclei of varying sizes and shapes.

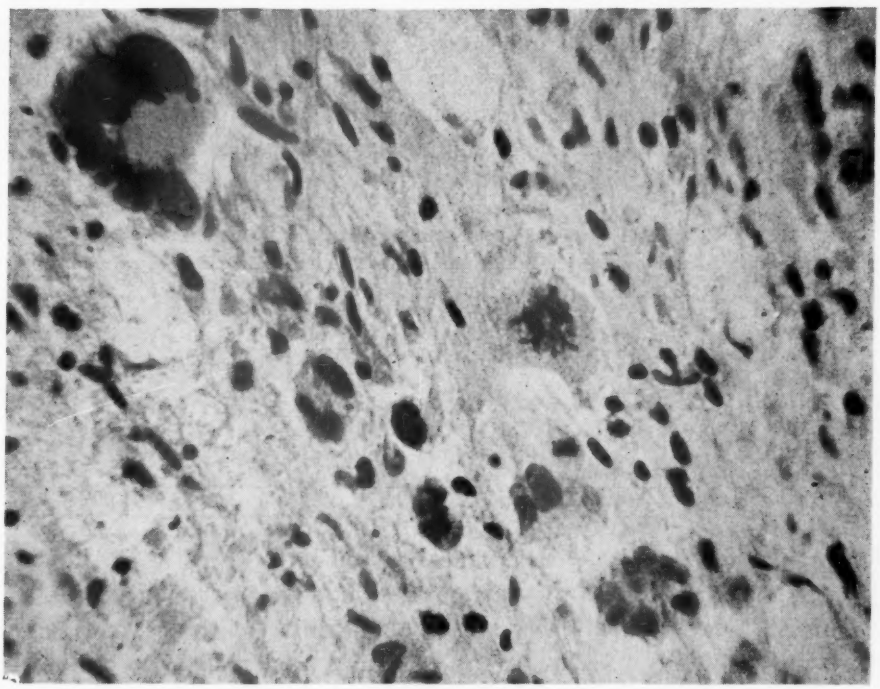


Fig. 11.—Rhabdomyosarcoma. Plasmodial-like syncytium cells in mitosis.

One of the most important features of rhabdomyosarcomas from a diagnostic viewpoint, is the presence of fibrils, chiefly cross striations. Although they have been described as occurring in all the cell types, most histologists have agreed that they are predominant in the spindle-cell syncytial arrangement. The transverse striations are perhaps most readily seen in the teratomas or mixed-cell tumors in which there are muscular elements as a part of the complex tumor mass, but the cross striations are truly seldom conspicuous in the cells of the rhabdomyosarcomas arising in skeletal muscles. Demonstration of these striations establishes the diagnosis of rhabdomyosarcoma with certainty, but unfortunately there exist many instances in which the fibrils cannot be demonstrated. Their demonstration, even when present, often requires an extremely skillful staining preparation and meticulous microscopic study. In 39 cases of rhabdomyosarcoma reported by Jönnson[20] he did not find fibrils in a single instance. In the absence of fibrils, the pathologist must depend on the

cellular components and structural arrangement in order to make the diagnosis. Complete and detailed descriptions of the histologic character of the rhabdomyosarcoma are given in the papers by Stout, Rakov, and Wolbach.

REGIONAL LOCATION

The approximate location of the rhabdomyosarcomas in each patient is shown in Fig. 12. The percentage distributions in the various locations are tabulated in Table III. The upper extremity including the shoulder was involved in 34 cases (34 per cent) and the lower extremity, including the buttocks and groin, was the site of the tumor in 54 cases (54 per cent). The regional distribution of rhabdomyosarcoma does not follow the pattern of most other soft part sarcomas inasmuch as there is a definite predilection for the lower extremity and particularly for the thigh muscles. In this series the individual muscles most often affected were the quadriceps, the adductor muscles of the thigh, the biceps, and the brachialis.

TABLE III. RHABDOMYOSARCOMA OF SKELETAL MUSCLES; LOCATION OF TUMOR

REGIONAL SITE	NUMBER	PER CENT
Hand	1	1
Arm	27	27
Shoulder	6	6
Leg	9	9
Thigh	41	41
Buttocks	3	3
Groin	4	4
Chest, back and abdominal wall	9	9
Total cases	100	100

Gordon-Taylor found the rhabdomyosarcomas to have a predilection not only for certain segments of the extremities but even for certain muscles. He quotes Durante who stressed the special vulnerability of the rectus femoris, the triceps of the arm, the muscles of the lower leg, especially the deltoid muscle and the glutei muscles. Rakov of Leningrad found 6 rhabdomyosarcomas occurring in the thigh, 3 in the arm, 4 in the shoulder girdle, 1 within the thorax and 1 in the lumbar region. One fact of uncertain significance which has appeared as a result of analysis in the present series is that the curability of rhabdomyosarcomas of the arm (45.5 per cent) is twice as great as for rhabdomyosarcomas of any other regional location.

Geschickter has commented properly on the extremely rare occurrence of rhabdomyosarcomas in the spinal muscles of the body wall which were derived from the paraxial mesoderm. This rarity of tumor formation, he thought, was probably dependent on the extremely early differentiation of these structures. T. M. Peery and W. A. Smith[31] reported the second case of primary rhabdomyosarcoma of the diaphragm; this occurred in a 14-year-old Negro boy on whom a necropsy was obtained.

Palumbo, Leibovitz, and Corcoran[30] collected 208 cases of rhabdomyosarcoma from medical literature and reported the distribution of these tumors as follows: skeletal muscles—121, epididymis—1, uterus—22, spermatic cord—1, prostate—18, urinary bladder—9, orbit—19, and testis—17.

Arthur Purdy Stout has made the statement that although the striated muscle tumors may occur most commonly within the skeletal muscle groups of the body, yet they may also be found sporadically in the genitourinary system, urinary bladder, kidneys, prostate, testis, spermatic cord, uterus, vagina, round ligament, ovary, heart, upper respiratory tract, gastrointestinal tract, and orbit.

The statistical analysis in the present dissertation is limited solely to the rhabdomyosarcomas involving the skeletal muscles but we have observed and treated our quota of these tumors occurring in orbit, prostate, spermatic cord, etc., examples of which will be cited with a brief description of the characteristic features of the tumors in these locations. They are not, however, included in the statistical studies of the rhabdomyosarcomas as a rule because the natural history, curability, and other features are not consonant with the greater group of skeletal muscle sarcomas.

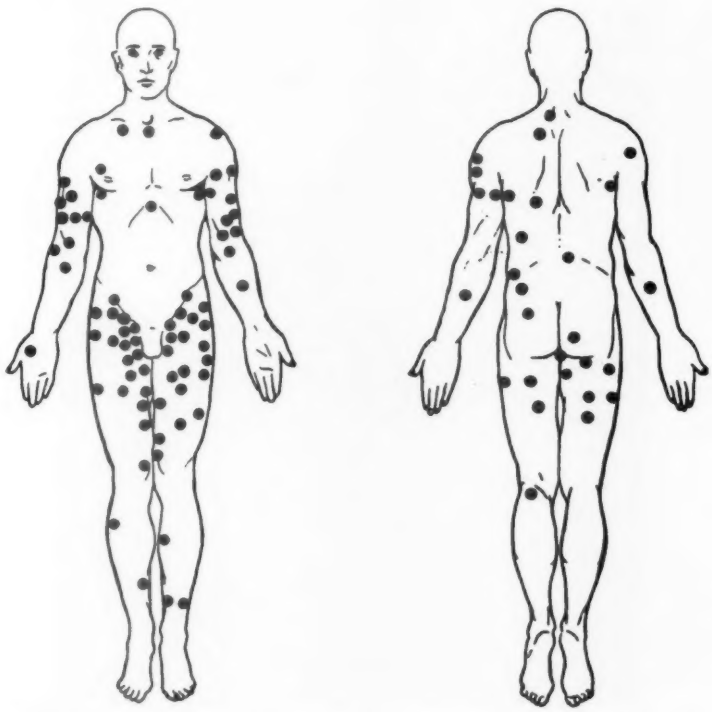


Fig. 12.—Scattergram illustrating regional distribution of rhabdomyosarcomas.

RHABDOMYOSARCOMAS OF THE HEAD AND NECK IN CHILDREN

Stobbe and Dargeon[39] have reported 15 cases of embryonal rhabdomyosarcoma of the head and neck in children and adolescents, from the records of the Memorial Hospital. These cases are not included in the series presented here, nor are they represented in the statistical analysis. These 15 children averaged 6 years of age with the youngest only 16 months old and the eldest 16 years. An equal incidence between the sexes was found and there was no apparent familial predisposition. The location of the tumor was: the orbit and

region of the internal canthus—4 cases, the tonsil and the soft palate—4 cases, the mastoid and internal ear—2 cases, with the remaining 5 neoplasms distributed in the regions of the neck, temple, zygoma, and parotid. The mean time interval between the onset of symptoms and the time of treatment was 3½ months. The initial complaints depended on the location of the primary tumor and in addition to the presence of the neoplasm were listed as dysphagia, abnormal phonation, cough, divergence of the eye, deviation of the jaw, and discharge from the ear. Six post-mortem examinations were available for review; metastases were discovered in cervical and mediastinal lymph nodes, lungs,

Fig. 13.—Rhabdomyosarcoma of the inner aspect of the thigh, the most common location of this tumor.

pleura, ovaries, peritoneum, vertebral column, femurs, kidney, uterus, pancreas, thyroid, and brain. Stobbe and Dargeon found frequent recurrences after excision, x-ray or radium therapy; the recurrences, often in multiple foci, appeared in 2 weeks to 1 year, usually within 3 months after the previous treatment. Two of the 15 children were living without recurrences for more than 11 years; their treatment had been radical surgery, supplemented by x-ray and radium therapy.

INTRAORBITAL RHABDOMYOSARCOMA

The intraorbital rhabdomyosarcomas are commonly tumors of childhood occurring usually in children under 10 years of age with an average age of 6 years. Calhoun and Reese[8] found the sex incidence to be 12 boys to 5 girls. The location is usually in the upper inner quadrant of the orbit, but occasionally may be retrobulbar and diffuse. They may originate too from the extraocular lid muscles.

Fig. 14.—Fungating recurrent rhabdomyosarcoma of the medial aspect of the left upper thigh.

The apparent encapsulation is of no value in prognostic evaluation because the circumscription is a pseudocapsule due to compression of the surrounding tissues. The tumor cells are pleomorphic, occasionally of giant size, and sometimes of spindle structure with ribbonlike ends, tinctorially resembling muscle cells. The nuclei are large. The eosinophilic cytoplasm contains fibrils which may or may not exhibit cross striations.

The young patients frequently die of generalized metastases. Conservative local excision of the tumor is commonly followed by recurrence. The orbital rhabdomyosarcomas are relatively radioresistant: one of our patients showed temporary clinical regression following fractionated doses of x-ray therapy administered through a small localized cone. Calhoun and Reese have advocated exenteration of the orbit and in 2 patients so treated, no local recurrence had developed. Forrest[13] reported 2 patients living and well, 10 and 14 years, respectively, after treatment.

MYOBLASTOMA OF ABRIKOSSOFF

In 1926, Abrikossoff described 5 peculiar muscle tumors which he termed myoblastic myoma. Three tumors were located in the tongue, 1 on the upper lip, and 1 on the leg. The cells of these tumors were believed to arise from the embryonal ancestors of voluntary muscle. Tumors of this type occur most commonly in the third and fourth decades of life; a few have been described as congenital in origin. The granular-cell myoblastomas have unusual distribution, occurring most commonly in the tongue, the lip, vocal cords, esophagus, and breasts. In a review of granular cell myoblastoma, Howe and Warren[19] were able to collect 158 cases from the literature to which they added 10 of their own. Fifty-six per cent of the tumors in their series occurred in the upper respiratory and digestive tracts. Fifty-nine cases, or more than a third, occurred in the tongue, which appears to be the most common site for muscle tumors of this particular type. In the tongue, the tumor is usually situated on the dorsal aspect or near the base and it is firm, discrete, yellowish or grayish-white on transection. Although the majority of the tumors are well demarcated and pseudoencapsulated, a few are infiltrative and ill defined in their margins. Myoblastomas occurring in the upper digestive or respiratory tracts are usually found immediately beneath the mucous membranes as a submucosal swelling.

Since the initial description of the granular-cell myoblastoma by Abrikossoff, this tumor has been generally accepted as one composed of immature myoblasts. Howe and Warren believe these tumors should be segregated as a group, separate from the rhabdomyomas and rhabdomyosarcomas. Abrikossoff originally separated the myoblastomas into four types depending on the cellular structures: (1) Pure myoblastoma tumors composed of myoblasts, completely devoid of striations. (2) Tumors with myoblasts as in type 1, but with imperfectly developed longitudinal or cross striations in the margins of the cells. (3) Tumors composed of hypertrophic myoblasts. Some of these cells attain great size, up to 160 μ in length. They are frequently multinuclear and of the syncytial type. Peripheral striations may or may not be present. (4) Atypical myoblastic sarcoma. This is a polymorphous-cell tumor. In some areas, it is frankly sarcomatous; in others it is highly differentiated with well-defined cross striations. Howe and Warren believe the tumors in this group to be really rhabdomyosarcomas.

The characteristic cell of the myoblastoma is a large, pale, polyhedral-shaped cell with acidophilic cytoplasm, which is occasionally vacuolated. These

granular cell myoblastomas in the oral cavity give the initial microscopic impression of xanthoma, because the large vacuolated cells in a myoblastoma are readily confused with the foam cells of xanthoma. Masson's trichrome stain is employed for differentiation inasmuch as the myoblasts and myofibril stain red in contrast to the green connective tissue fibers.

Fig. 15 (Case 2).—Benign granular myoblastoma of the tongue.

The granular-cell myoblastomas are generally benign tumors. Howe and Warren reported only 11 per cent of their total series to be malignant, and of these, only 3 had definitely metastasized. The common manifestation of malignancy when this rare complication does occur, seems to be local invasion and recurrence after simple excision rather than dissemination by lymphatic or blood stream permeation. Howe and Warren urge that myoblastomas of this type be treated as malignant tumors if there is cellular atypia, excessive mitotic figures, spindle-cell or sarcomatous pattern and structure, or local invasion. The treatment of preference is wide surgical excision.

CASE 2. Benign Embryonal Myoblastoma of Tongue (Abrikossoff's Tumor).—C. T., a 12-year-old girl, had been aware of a swelling at the base of the tongue for 6 months

prior to the date of admission to the hospital. Four days before admission she expectorated blood which was followed later by hematemesis in large quantity. Bleeding occurred intermittently for 4 days and was extremely difficult to control.

On admission, a huge tumor 5 by 6 by 4 cm. was found occupying the base of the tongue posterior to the circumvallate papillae. It extended far down into the hypopharynx and partially occluded the oropharynx. A bilateral ligation of the external carotid arteries was performed. The tumor at the base of the tongue was enucleated without difficulty. A temporary tracheostomy was inserted. The defect in the tongue was closed by interrupted catgut sutures. The pathology report was embryonal myoblastoma of tongue, benign. There has been no recurrence in the succeeding 6 years.

RHABDOMYOGENIC TUMORS OF THE HEART

Von Recklinghausen, in 1862, first reported a congenital rhabdomyoma of the heart. This tumor occurs most often in the newborn and in children. In a review of the literature, Labate[24] collected 51 cases of which 46 occurred in patients younger than 15 years. In data presented by Batchelor and Maun,[5] 52 per cent of the patients were reported to have died in the first year of life and 86 per cent before the age of puberty. The rhabdomyoma of the heart occurs with equal frequency in the sexes and has been reported in Negroes and Japanese as well as Caucasians. This tumor is almost always associated with some other congenital anomaly, such as harelip, cleft palate, cystic kidneys, sebaceous adenomas, malformations of the pancreas, and most frequently of all, tuberous sclerosis of the brain (50 to 60 per cent) according to Ponfick.[33]

Ante-mortem diagnosis is seldom made because the clinical symptoms are nonspecific. Cardiac arrhythmias, disturbances of the conductive system of the heart, cyanosis, and detectable murmurs are heard if the tumors involve the valvular leaflets. Epileptiform seizures and other symptoms referable to the central nervous system might be anticipated in view of the commonly associated tuberous sclerosis.

The rhabdomyoma of the heart is a benign lesion and malignant transformation has not been recorded. Batchelor and Maun have suggested that the term "congenital nodular glycogenic tumor of the heart" should replace the term "congenital rhabdomyoma." Steinbiss[38] contends that these lesions should not be designated nor regarded as true neoplasms, because they do not exhibit proliferative activity, and degenerative changes such as fibrosis and calcification have been observed in the older lesions. Farber[12] also considers the disease to be a malformation rather than a true tumor. The diffuse type of rhabdomyomatosis of the heart has been considered a form of Gierke's glycogen storage disease. Monckberg[25] demonstrated glycogen in the tumor cells. Wolbach,[45] employing phosphotungstic acid—hematoxylin stain, demonstrated beginning muscle fibrillae formation, which influenced him to label the rhabdomyoma a true neoplasm. Abrikossoff, Monckberg, and Knox and Schorer[23] were of the opinion that the tumor cells originated from the Purkinje fibers, but Steinbiss, Amersbach and Handorn[4] claimed that the tumors were found most often where the conduction system could not be demonstrated. Von Recklinghausen, Seiffert,[37] Ponfick, and others have recognized a similar appearance of these tumor cells to the embryonic heart muscle cells.

These tumors of the heart of disputed character may be subepicardial, intramural or subendocardial, occurring in any part of the heart including the valves, and more frequently in the left ventricle. They may be single or multiple and appear as discrete or diffuse, white, soft homogeneous foci. The interlacing bundles of cardiac muscle fibers are distended and infiltrated by the tumor tissue. Under the microscope, the so-called spider cells are many-processed cells lying within vacuolated regions. Some histologists consider these highly characteristic spider cells as huge embryonic cells but Batchelor and Maun assert that the spider cell "represents a striated muscle cell that has become vacuolated by intra-cellular accumulations of glycogen in such a manner that the nucleus of the cell remains centrally located surrounded by a narrow zone of cytoplasm while the remaining cytoplasm assumes a spider web pattern."

RHABDOMYOMATOUS TUMORS OF THE URINARY BLADDER AND PROSTATE

In lower animals, the urinary bladder is one of the most frequent sites of visceral rhabdomyomatous tumors. Cappell and Montgomery have described 2 distinct forms of striped muscle tumors of the urinary bladder. The more frequent type is a polypoid tumor with bulbous processes, suspended from a common stalk and analogous in its gross, and perhaps in its embryologic, relationships to the vaginal sarcoma botryoides. Both longitudinal and cross striations are present in the muscle cells which may be of the strap-cell type or large cells with vacuolated cytoplasm resembling spider cells. The second variety is a mushroom-shaped tumor with broad stalks which Cappell and Montgomery have found to originate usually from the bladder trigone.

The origin of rhabdomyomatous tumors of the urinary bladder and prostate is uncertain, but the theory is that they may have arisen from displaced myotomes associated with descent of the wolffian duct.

The following case report illustrates rhabdomyosarcoma of the prostate gland. Striated muscle tissue is present in the posterior superior portion of the prostate gland of the fetus and in children; presumably, it is from this site that the rhabdomyomatous tumors of the prostate develop in later life.

CASE 3. Rhabdomyosarcoma of Prostate.—G. E., a 47-year-old man, had symptoms of prostatic enlargement with partial urinary obstruction in January of 1940. A two-stage suprapubic prostatectomy was performed. The prostate contained a soft tissue tumor pronounced by Dr. Fred Stewart to be a rhabdomyosarcoma. Fourteen months after the date of operation he complained of urinary frequency and a sensation of pressure within the rectum.

On physical examination he was found to be a vigorous man in apparently good general health. On rectal examination a bulky, lobulated, semifixed tumor was palpated in the region of the prostate where it projected into the rectal ampulla and invaded the rectal wall. A roentgenogram of the chest revealed no evidence of pulmonary metastasis.

The choice of treatments at that time was either to do a total cystectomy and abdominoperineal rectal resection with ureteral implantations or to rely on combined external and interstitial irradiation.

Employing the million-volt x-ray apparatus with 2 mm. of mercury and 8 mm. of copper filter, 70 cm. target-skin distance, 3 Ma. of current, with treatment to 3 ports, namely, left pelvis posteriorly, right pelvis posteriorly, and direct suprapubic fields, giving

300 r. daily and alternating, a total dose of 3,000 r. × 3 was administered, supplemented by a perineal port with fractions of 300 roentgens for a total dose of 2,100 roentgens. Under spinal anesthesia and with finger guidance in the rectum the bulky tumor was implanted with 53 mc. of radon in gold seeds through the perineum. Regression was immediate and apparently complete.

The tumor completely regressed but as an end result of its solution, a rectovesical fistula resulted which required a colostomy and a retention catheter. The patient gained in weight and was in very good health until July, 1944, when he was treated for arterial hypertension, arteriosclerosis, dilation of the aorta and the anginal syndrome. He died of heart disease in March of 1945 with no evidence of recurrence of the prostatic sarcoma and no evidence of pulmonary metastasis on the date of death. The period of survival without recurrence was 4 years subsequent to his last radiation treatment.

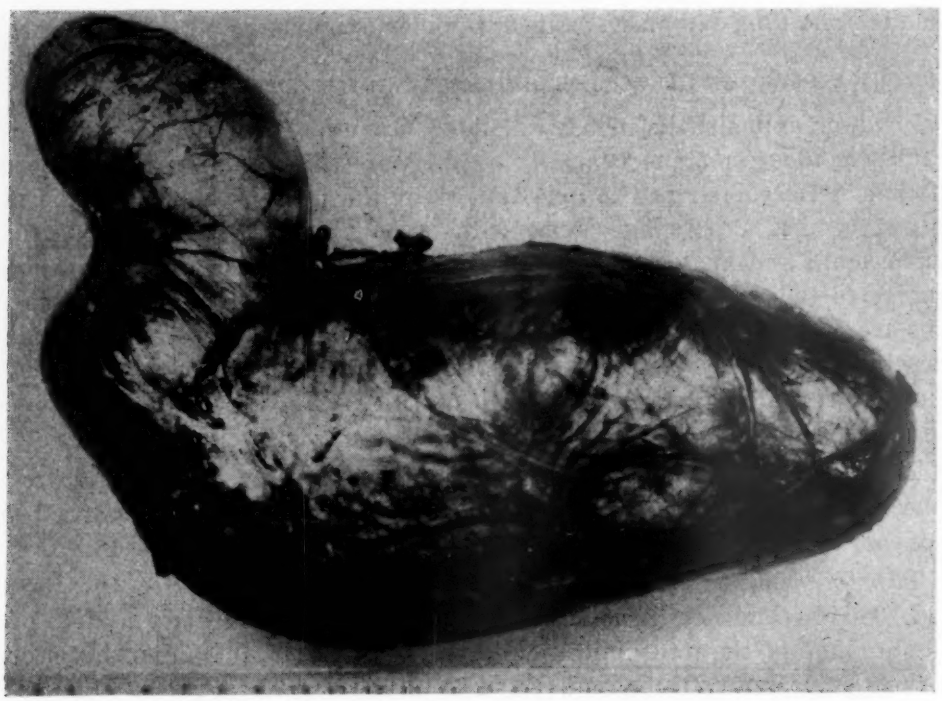


Fig. 16 (Case 4).—Benign myoma of gubernaculum.

MYOBLASTOMAS OF THE SPERMATIC CORD AND GUBERNACULUM

These rare muscle tumors are seldom mentioned in medical literature; we are contributing 2 case reports of this unusual occurrence (Cases 4 and 5). The genesis of primary rhabdomyomas of the spermatic cord is uncertain: Stoerck[40] and Monckberg independently observed instances in which the neoplasms arose in the vas deferens. Hirsch[18] reported this occurrence in the gubernaculum testis. Inasmuch as these structures are composed of smooth muscle fibers, the neoplasms would naturally be expected to contain unstriped muscle cells, but this supposition is not always true as the cells occasionally may exhibit cross striations.

CASE 4. Myoma of Gubernaculum Testis.—J. R., a 59-year-old man, had been aware for two months of a discomfort in the right lower abdomen. He later observed a mass

in this region which slowly increased in size. On examination, the right testis was missing and presumably was situated intra-abdominally. A huge mass was felt in the right iliac quadrant and a presumptive diagnosis of retroperitoneal tumor was made. At laparotomy, a sausage-shaped, encapsulated, retroperitoneal tumor was found in the right iliac qaudrant; its only point of attachment was near the right inguinal ring. It was dissected intact. It measured 28 by 11 by 11 cm. in diameter. On section, it consisted of a large cyst cavity filled with dark chocolate-colored fluid; projecting within the cyst were numerous lobular tumors, the largest measuring 5 by 5½ by 7 cm. They were coarsely fasciculated. On microscopic examination, no testicular tissue was discovered and no evidence of any teratoid tumor of an intra-abdominal testis. The tumor was comprised of an adult type of smooth muscle resembling a uterine myoma. The tube-like structure along the side of the tumor was the spermatic cord. The presumptive diagnosis was myoma of the spermatic or gubernaculum testis. The tumor was classified as benign.

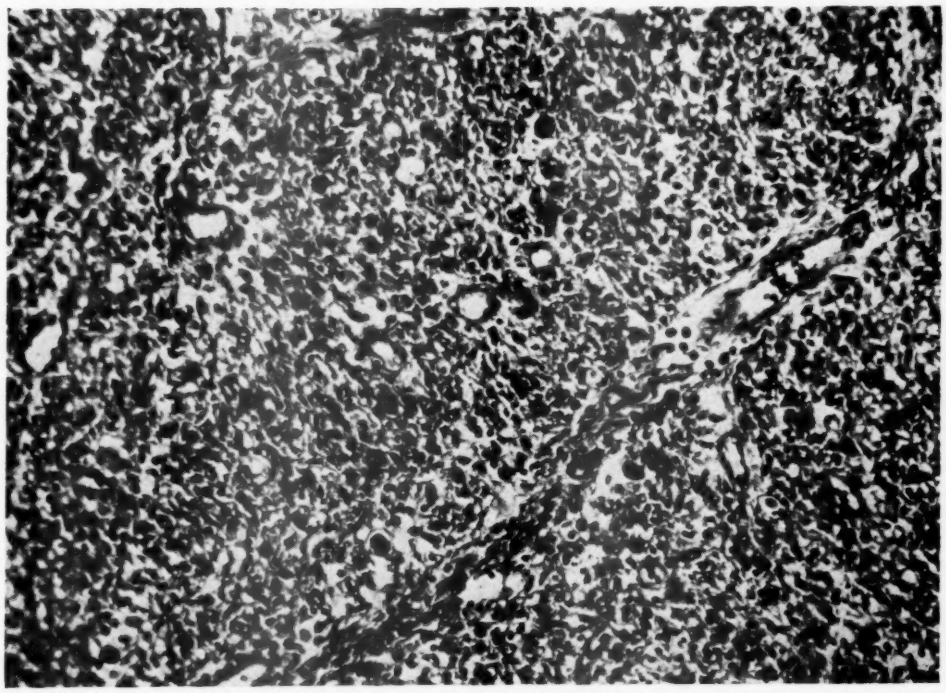


Fig. 17 (Case 5).—Retroperitoneal embryonal rhabdomyosarcoma in a child.

CASE 5. Retroperitoneal Embryonal Rhabdomyosarcoma of Gubernaculum.—E. L., a 5-month-old baby, was admitted to the hospital with a huge tumor situated in the lower abdomen and pelvis, extending up to the umbilicus and as far as the midline. A barium enema and roentgenograms of the colon revealed situs inversus. The large bowel was displaced medially by the tumor. Intravenous pyelography demonstrated extrinsic pressure on the left ureter with resultant hydronephrosis and hydroureter. A previous attempt at surgical excision in another institution had been unsuccessful. Because of the proved radioresistance of the tumor, a second attempt at radical surgical dissection was made. The neoplasm was intimately adherent to the testis, but the testis was not a part of the true tumor. The diagnosis was embryonal rhabdomyosarcoma presumably originating from the gubernaculum testis. Within 2 months a recurrence developed deep in the pelvis and involved the urinary bladder fungating into the cavity, causing obstruction of both ureters, and death from uremia.

DIAGNOSIS OF RHABDOMYOSARCOMA; SIGNS AND SYMPTOMS

On theoretical grounds, the tumors of skeletal muscle would seem so readily accessible that early diagnosis and definitive treatment would be the rule. The contrary pattern of action apparently is due to the fact that the tumor is usually of silent growth. Pain is an infrequent complaint and occurred in only 17 patients in this series of which only one experienced discomfort in severe degree. Usually the ache or discomfort resulting from a deep-seated muscle tumor is dismissed as a "stretched muscle" or a "charleyhorse" with corresponding treatment, that is, massage, diathermy, etc. Gordon-Taylor has commented on the significant frequency of the insidious onset and development of these tumors. He has observed that they betray their appearance many times in the form of a painless localized swelling; the absence of pain, the negligence of the average patient regarding a lump which does not interfere with normal activities, or the fear of an unpalatable surgical opinion, tending to keep the operator and victim apart until the tumor has often attained a considerable size. Interference with function of the affected extremity is a late manifestation and may be in marked contrast to the size of the tumor. Limitation of motion may occur only when the tumors are located in close proximity to the joint and the onset of early pain is more likely to occur whenever the neoplasms are situated adjacent to a nerve trunk.

There is a considerable variation in the clinical appearance of the tumor. The neoplasm may be located superficially and appear to be discrete, encapsulated, and freely movable. On the other hand, there may be a deep-seated, fusiform mass producing distortion of the involved muscle or muscle groups. If the involved muscle can be made to relax, the tumor will usually be movable in all directions. This mobility characteristically disappears when the muscle is contracted. Changes in mobility with relaxation or contraction of the muscle are an important feature and point to a muscular localization of the tumor. The skin and subcutaneous tissues immediately overlying the tumor are usually unchanged. There may be a fine network of dilated veins. In a few instances the tumor infiltrates the skin and gradually produces pressure necrosis, ultimately leading to a mushroomlike, ulcerated, bleeding cutaneous mass.

DIFFERENTIAL DIAGNOSIS

In the differential diagnosis of rhabdomyosarcoma involving skeletal muscles, there are a number of different lesions which simulate this neoplasm. Among them, of course, are the numerous varieties of malignant and benign tumors of the soft somatic tissues of varied histogenesis. Even a deeply situated lipoma may be confused with rhabdomyosarcoma because of its firmness on contraction of the surrounding muscle groups. Aspiration biopsy or the demonstration of the translucence of the deep lipoma on roentgenography are practical distinguishing features. Intramuscular cysts and unresolved deep hematomas are sometimes extremely difficult to distinguish from rhabdomyosarcomas because the latter lesion occasionally undergoes intratumoral hemorrhage with infarction and necrosis. Muscle angiomas have always been diagnostically confused with

this tumor except for the fact that they commonly cause more discomfort, usually show calcium depositions in the substance of the neoplasm, and increase in volume on motion of the affected part.

Tumors of the skeletal muscles would seem to be so accessible that early diagnosis and treatment would be the rule but unfortunately their deep location and the usual absence of pain and disability conspire to delay the diagnosis until the lesion has often reached bulky dimensions. This asymptomatic and non-disabling presenting mass usually deeply situated is the common way in which the tumor heralds its appearance. The deeply situated rhabdomyosarcomas may give the false impression of immobility, but they are seldom fixed; the probable explanation lies in the origin or insertion along the bone of the involved muscle groups. The mobility of the tumor when the muscle is relaxed and the immobility when the muscle is contracted has been accepted by numerous authors. There is very little mechanical interference with muscular function until the tumor perforates the sheath of the muscle and by invasion becomes attached to adjacent fixed structures. As a rule, skin and superficial tissues move over the tumor and the tumor moves over the underlying bone. In commenting on the fact that the rhabdomyosarcoma changes in position with contraction (shortening) and relaxation (elongation) of muscle, Bick has stated a law which is pertinent and acceptable: "The amplitude of change in position during muscle activity diminishes as the situation approaches the functional mid-point of the muscle, and increases as it is distant from that point."

THE RATE OF GROWTH OF RHABDOMYOSARCOMAS

The clinical course of this tumor falls into one of three growth patterns as originally noted by Gordon-Taylor: (1) The neoplasm may remain small and quiescent for many months or even years and then suddenly exhibit an exacerbation of growth which may be spontaneous or possibly induced by trauma. (2) The tumor may grow in a fulminating acute manner from its onset, metastasize early, be recalcitrant to any form of treatment, and cause death within a short time. (3) The rhabdomyosarcoma may grow slowly for weeks or months. The hazard in this last instance lies in the inducement to operate too conservatively so that an unnecessarily large number of recurrences develop.

Harper and Feder[17] record an unusual instance of a rhabdomyosarcoma occurring in the sternocleidomastoid muscle of a 75-year-old Negro, which tumor had existed for 50 years without growth, then rapidly enlarged; the microscopic diagnosis was made by James Ewing. In one of our patients the tumor was known to have been present 11 years before treatment was instituted.

Some interest attends the duration of time between the appearance of the first symptom or sign of a mass and the first visit to a physician. The failure to see a physician is due in all probability to the characteristic lack of pain and to the equally characteristic failure of the tumor to produce dysfunction of the part. A third deterrent is undoubtedly the fear of an unpalatable surgical opinion. In the present series a statement of the known duration of the

tumor before initial treatment was available for 95 patients (Table IV). A perusal of this table shows that the patients dying of rhabdomyosarcoma came 4 months earlier for treatment than those patients who were cured. This paradox is readily understandable, because the more highly malignant sarcomas grow more rapidly and induce greater apprehension in the patients.

TABLE IV. RHABDOMYOSARCOMA OF SKELETAL MUSCLES; HISTORY OF DISEASE PRIOR TO INITIAL TREATMENT

TYPE OF CASE	AVERAGE IN MONTHS
Patients living now	8.7
Patients who died of rhabdomyosarcoma	4.7
Patients dead of other causes or lost to follow up	7.7
Recent group	6.9
Total cases	6.6*

*Excludes one patient with a history of 11 years.

METASTASES

It is surprising that metastases do not consistently occur, if we consider the fact that the muscles contract forcibly and often on the enclosed sarcoma. It is not the large myoblasts with striated fibers that usually are disseminated but the more primitive, anaplastic, round and spindle cells which metastasize to distant sites where they differentiate after implantation (Cappell and Montgomery). The mode of extension plays some role in the diffusion of the sarcoma, particularly its local growth, where it spreads more readily along the fascial planes than it does along the intermuscular spaces.

The rhabdomyosarcomas have an abundant vascular supply and tend to metastasize early to the lungs, which are by far the most frequent site for metastases. In 39 out of 41 of our unsuccessful cases there was positive x-ray evidence of pulmonary metastases. Generalized metastases (bone, skin, brain, viscera) are rare but the spinal column is sometimes secondarily involved.

It is not generally known that sarcomas of striated muscle can and do metastasize through lymph vessels to regional lymph nodes. In our series of 100 patients this occurred 6 times (6 per cent). The metastases in lymph nodes are prone to undergo necrosis and hemorrhage; the tumor tissue within the nodes has an alveolar architecture which simulates anaplastic carcinoma and may be erroneously diagnosed as such.

CASE 6. Rhabdomyosarcoma of Vulva Metastatic Bilaterally to Groins.—C. L., a 47-year-old woman, was first seen on July 25, 1949. Four years before (June, 1945), a tiny, deep, spherical tumor was felt in the left vulva by the patient. It gradually grew in size until November, 1945, when the labium minus was surgically excised with the contained tumor. It was diagnosed as rhabdomyosarcoma. Nine postoperative x-ray treatments were immediately given. She was free of symptoms for 2 years until November, 1947, when she experienced discomfort in both groins. In March, 1948, palpable inguinal masses were felt and these enlarged lymph nodes were surgically dissected by another surgeon. An interval of freedom existed until March, 1949, at which time severe pain

occurred, particularly in the right groin. In June, 1949, large masses were palpable in both groins. The overlying skin showed the effect of chronic radiation dermatitis. The masses involved the deep inguinal and femoral lymph nodes. They were semifixed.

The diagnosis was recurrent rhabdomyosarcoma of vulva with bilateral metastasis to inguinal lymph nodes.

The treatment given was radical vulvectomy with bilateral groin dissection. The entire vulva was surgically excised, together with a wide segment of skin of both groins, to include the underlying fat and fascia, and all the lymph nodes in the femoral, inguinal, and deep iliac groups. The inguinal ligaments were transected and the dissections carried out retroperitoneally to the bifurcation of the aorta. The operation was done by excision and dissection in continuity.

Pathology Report.—The site of the primary tumor contained no recurrent cancer. The lymph nodes in the groin were involved by rhabdomyosarcoma. The deep iliac nodes were free of evidence of metastasis.

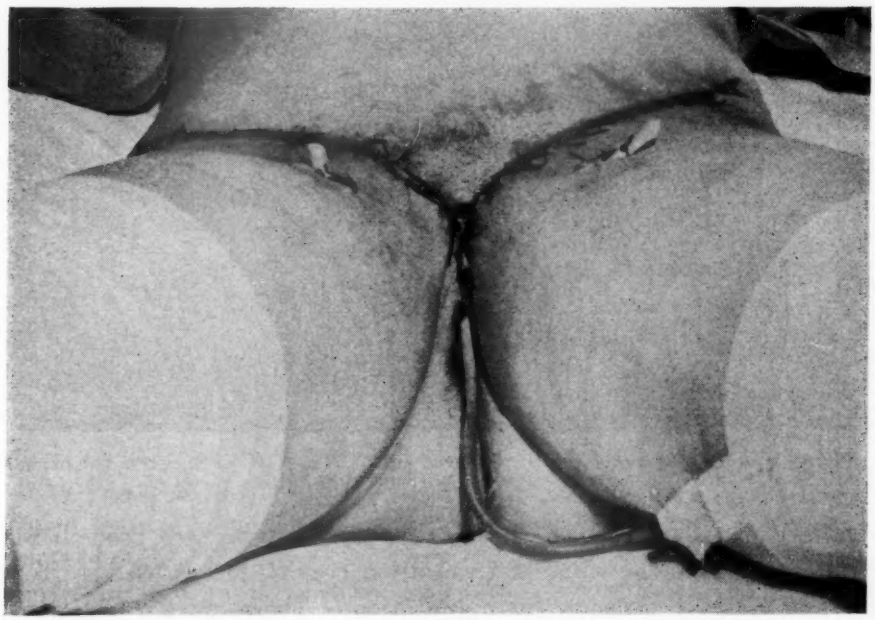


Fig. 18 (Case 6).—Rhabdomyosarcoma of the vulva, metastatic bilaterally to inguinal lymph nodes. Operative wound following radical vulvectomy and bilateral groin dissection.

RADIOSENSITIVITY AND RADIATION THERAPY OF RHABDOMYOSARCOMAS

Radiation therapy alone is not sufficient to sterilize the average rhabdomyosarcoma; such treatment is often followed by necrosis and hemorrhage into the body of the tumor, and later reactivation and diffuse invasive growth. Rhabdomyosarcomas are relatively radioresistant. Postoperative irradiation by the fractionated dose principle has been advocated and employed as an adjunct to radical local dissection on the principle of inducing sufficient additional interstitial fibrosis throughout the operative site as to inhibit or delay any tendency to recurrence. There have been some instances in our experience wherein preoperative irradiation has converted a technically inoperable sarcoma to one which was successfully removed; 2 of these patients are living and well

more than 10 years since the dates of operation. It is superfluous and procrastinating to administer preoperative irradiation, if the surgeon contemplates an amputation of the extremity. Therefore, we may say that radiation therapy should never delay surgical treatment if the sarcoma is operable; radiation therapy should never be substituted for surgical treatment so long as a cure remains possible.

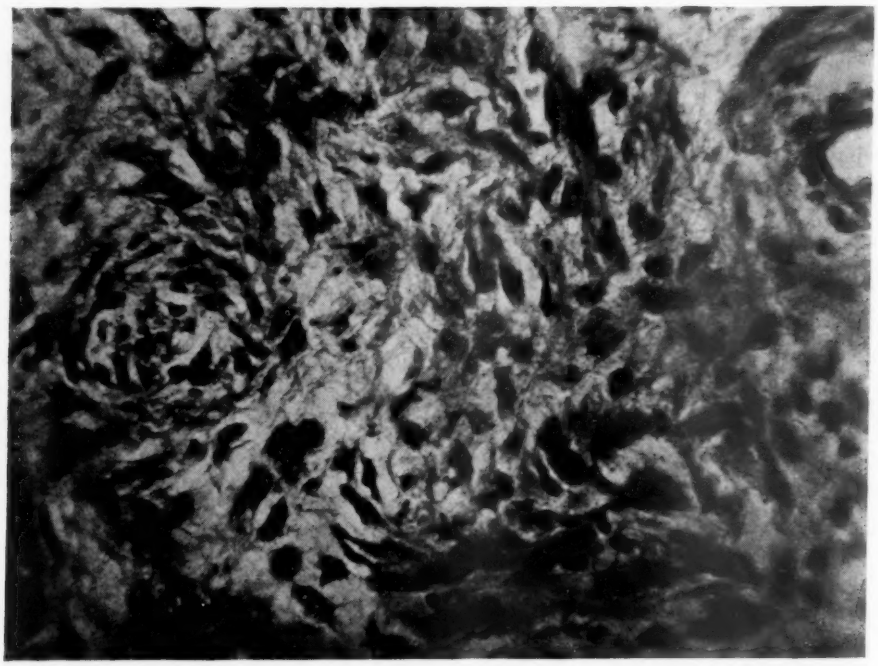


Fig. 19 (Case 6).—Rhabdomyosarcoma of the vulva. Part of a complex tumor exhibiting some features of sarcoma botryoides.

Irradiation, either alone, or pre- or postoperatively, was used in 61 cases. It is difficult to assess the value of irradiation because it was used so frequently in combination with excision or amputation. There were 11 patients who received preoperative irradiation in the form of x-rays or radium element pack; in 9 of these patients there was definite local recurrence of tumor or the surgically excised specimen showed viable tumor cells. Forty-four patients received some type of postoperative irradiation, 25 of them developed definite local recurrence following completion of the irradiation. On the basis of these data, we can say that these tumors are not radiosensitive and irradiation cannot be depended upon to prevent local recurrence when it is given following an inadequate local excision.

THE SURGICAL TREATMENT OF RHABDOMYOSARCOMAS

Treatment in these patients has consisted of surgical excision, irradiation (preoperatively and postoperatively), radium in the form of radium element pack or radium needles, and amputation. These therapeutic methods have been used singly and in various combinations. A glance at our tabulation shows that

very few patients were treated exclusively by one form of therapy. Surgical excision as the initial method was done in a total of 58 cases (all groups included). In 7 patients it was the only treatment. The remaining patients had additional therapy in the form of postoperative irradiation, amputation, or a combination of both.

SURGICAL DISSECTION OF RHABDOMYOSARCOMAS

The choice between radical surgical dissection and amputation depends on innumerable factors such as the degree of malignancy, the regional location, the fixity or mobility, the primary or recurrent status, the presence of regional and distant metastases, and most important, perhaps, the experience and judgment of the operator.

Before a course of action is decided, the histologic diagnosis should be established. If the sarcoma is recurrent, the original specimen is available for detailed study and special staining. If the neoplasm has not been previously treated and the clinical features or aspiration biopsy have not been revealing, a formal incisional biopsy is done under tourniquet control and with frozen section analysis. The immediate diagnosis is followed at once by positive action, either surgical dissection or amputation. It follows that the surgeon should be equipped with knowledge of the behavior patterns of the various sarcomas, for example, the tendency of angiosarcomas to metastasize to lungs via the venous system, the surprising frequency of lymph nodal involvement by synoviomas, and the almost irrepressible impulse of fascial sarcomas to recur locally. To minimize the degree of surgical trauma, consent for amputation should be obtained prior to the preliminary exploration.

Many sarcomas are soft, cellular, anaplastic, and vascular, and sustain the reputation at least of metastasizing readily with slight trauma. If such a tumor is to be attacked directly by local removal, the dissection should be performed gently with meticulous care and retraction should always be away from, rather than toward, the tumor. The soft tissues encompassing the lesion should never be compressed or handled roughly. If the rhabdomyosarcoma is located on an extremity, a tourniquet is applied proximally well above the tumor. It remains in place while the biopsy is being done, and during the subsequent local removal. If the attempt at local removal fails, whether because of technical difficulties or because the surgeon realizes the futility of the effort, an immediate amputation is performed above the level at which the tourniquet remains applied.

Gross and microscopic study of the veins removed with the specimen not infrequently reveals the presence of intravascular tumor thrombi, which theoretically might easily have been dislodged during the trauma of the operation or could have propagated centripetally into larger venous channels. On several occasions we have removed masses in the femoral trigone under the clinical diagnosis of metastatic sarcoma in lymph nodes, only to find that the sarcomas were tumor thrombi growing in the larger venous tributaries. These observations have influenced our associate, Dr. Robert Booher, in formulating a prin-

TABLE V. RHABDOMYOSARCOMA OF SKELETAL MUSCLES; OPERABILITY ACCORDING TO YEAR OF ADMISSION

TYPE OF CASE	TOTAL CASES		1928 TO 1933		1934 TO 1938		1939 TO 1943		1944 TO 1948	
	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
Cases receiving definite treatment	75	75.0	2	66.7	22	73.3	32	72.7	19	82.6
Primary operable cases	24	24.0	0	0.0	7	23.3	9	20.4	8	34.8
Recurrent operable cases	45	45.0	0	0.0	11	36.7	23	52.3	11	47.8
Cases receiving postoperative prophylactic x-ray therapy (surgery performed elsewhere)	6	6.0	2	66.7	4	13.3	0	0.0	0	0.0
Cases receiving palliative treatment or none	25	25.0	1	33.3	8	26.6	12	27.3	4	17.4
Primary inoperable cases	7	7.0	0	0.0	4	13.3	2	4.5	1	4.3
Recurrent inoperable cases	7	7.0	1	33.3	1	3.3	4	9.1	1	4.3
Cases refusing treatment	11	11.0	0	0.0	3	10.0	6	13.6	2	8.7
Total cases	100	100.0	3	100.0	30	100.0	44	100.0	23	100.0

TABLE VI. RHABDOMYOSARCOMA OF SKELETAL MUSCLES; LOCATION OF TUMOR IN RELATION TO FIVE-YEAR SURVIVAL WITHOUT DISEASE

LOCATION OF TUMOR	CASES THROUGH 1943			5-YEAR SURVIVALS		DISTRIBUTION OF DETERMINATE CASES						
						PRIMARY OPERABLE		RECURRENT OPERABLE		PROPHYLACTIC IRRADIATION		IN-OPERABLE
	ALL CASES	INDETERMINATE CASES	DETERMINATE CASES	NUMBER	PER CENT (BASED ON DETERMINATE CASES)	NUMBER	5-YEAR CURES	NUMBER	5-YEAR CURES	NUMBER	5-YEAR CURES	NUMBER
Arm	22	4	18	10	55.6	3	1	12	8	1	1	1
Shoulder	5	1	4	2	50.0	0	0	4	2	0	0	1
Leg	6	1	5	2	40.0	2	0	2	1	1	1	0
Thigh	36	5	31	5	16.1	7	1	11	2	4	2	9
Buttocks	2	0	2	1	50.0	1	1	1	0	0	0	0
Groin	2	1	1	1	100.0	1	1	0	0	0	0	0
Chest, back, abdominal wall	4	0	4	1	25.0	2	0	1	1	0	0	1
Total cases	77	12	65	22	33.8	16	4	31	14	6	4	12

ciple for the routine ligation of either the axillary, superficial, or deep femoral veins prior to the local dissection and removal of sarcomas of the extremities. If such ligations are valuable prophylactically in the case of ordinary phlebothrombosis, they should be even more so if they can delay or stop the systemic dissemination of sarcomas of the extremities.

If the region of the tumor has been explored but the lesion not removed, if a formal incisional biopsy has been done, if a previous excision has been followed by recurrent growth of the residual tumor, or if fungation of the sarcoma has developed through the wound and the surgeon nevertheless decides that he will attempt a radical dissection, the one imperative technical necessity is that a wide encompassing elliptical excision of skin be made far beyond the limits of the original scar. Not only the scar in the skin but the scarred tract of the incision down to the tumor must be removed in continuity with the sarcoma because of the very real danger of implanted tumor cells within the previous incision. Some sarcomas grow under tension within their capsule or pseudocapsule and a break in this barrier may encourage unrestrained growth of the neoplasm along the cleavage plane of the incision.

Although not always possible of achievement, a good rule to follow is to remove the sarcoma without seeing or encountering it; by this we mean that the investiture of the neoplasm by muscles, fat and fascia remains inviolate and that the line of dissection is grossly well beyond the palpable limits of the tumor in all directions. Many sarcomas are spherical, oval, encapsulated or pseudoencapsulated and the temptation simply to enucleate them is great; the ease with which such tumors can be shelled out and their apparent complete localization gives the surgeon a false sense of security. Myomectomy is always too conservative. In the compromise of selecting local removal over amputation for these malignant tumors, the surgeon should not relax his vigilance in accepting simple enucleation as an easy substitute for the always essential radical dissection. In more recent years we have routinely removed the entire group of muscles involved by, or encompassing, the sarcoma from their origins to their insertions. This precaution is especially warranted in the case of the rhabdomyosarcomas and intermuscular liposarcomas. If the sarcoma is on the extremities, the order of the dissection is from above downward, that is, disengaging the superior limits of the tissue dissection first. If the rhabdomyosarcoma is situated near the attachments of muscle or fascia to bone, we invariably remove the periosteum at this site and in some instances chisel away the cortex of bone. Our past experience has led us to believe this lessens the hazard of local recurrences.

In these radical local removals, ruthless removal of adherent or implicated arteries and nerves is practiced. In the case of sarcomas of an extremity, partial loss of function is not too great a price to pay, in lieu of amputation, for the preservation of the limb in the treatment of an otherwise lethal disease.

Rhabdomyosarcomas of the chest wall should be attacked most aggressively at the initial attempt in an all-out effort to cure, inasmuch as one cannot resort to amputation if recurrence develops. Because of adherence to ribs or inter-

costal extension of the sarcoma, radical removal of large segments of the thoracic bony cage is occasionally necessary, but the resultant wound can be closed by thoracoplastic measures. Rib resections, sliding skin flaps, transposed muscle groups, free fascial transplants, and tantalum mesh can close the surgical defects. The same technical difficulties are encountered in the surgical treatment of sarcomas of the abdominal wall. The surgical excision of some sarcomas of the abdominal parietes is a formidable undertaking, requiring the sacrifice of large muscle groups and fascial planes; in many patients the entire thickness of the abdominal wall must be excised and the problems of wound closure are troublesome. In another paper we have reviewed our experience with approximately 400 tumors of the abdominal wall.

PRINCIPLES OF AMPUTATION FOR RHABDOMYOSARCOMA OF THE EXTREMITIES

In each individual case, there is a constant battle of judgment between the wisdom of the more radical amputation and the need for preservation of an important functional part. So many factors interplay here, such as the regional involvement by the tumor, its primary or recurrent status, the degree of malignancy, its encapsulation or infiltrative method of growth, that no set formulary for management can be established. Experience will continue to influence the operator in every circumstance. The recurrent rhabdomyosarcomas, the diffusely invasive sarcomas of striated muscle, and those which are so deeply adherent that a local excision is not feasible, are best treated by amputation.

As an example, an encapsulated rhabdomyosarcoma involving the central segment of the hand has been successfully removed by us with a modified amputation of the hand. The central segment of the hand with attached fingers may be amputated by metacarpocarpal disarticulations. The preservation of the thumb and fourth and fifth, or even only the fifth, fingers leaves a "lobster-claw" hand which by practice and adaptability becomes an extremely useful member. For grasping, the retention of the opposing thumb is most essential.

Amputation through the forearm for rhabdomyosarcomas totally involving the hand and wrist permits cineplastic procedures with utilization of muscular and tendon functions and a serviceable artificial hand, as has been done so well by Kessler. The upper levels of severance must be high, if not extreme, as related in the sections dealing with arm and leg amputations. The general rule of amputating above the level of origin of the muscle groups involved by the sarcoma is a good principle to observe. The arguments supporting this thesis may be adumbrated in the following brief summary:

a. The rhabdomyosarcomas may be multicentric, and palpable tumor nodules may exist in superior segments of the muscle, only to grow and be discovered later if the muscle is not entirely removed.
b. Many sarcomas extend imperceptibly high along the muscular and fascial planes.

c. The diffuse myogenic and fascial fibrosarcomas certainly must be removed above the level of the fascial attachment to bone. Even to leave the periosteal base at this site increases the hazard of recurrence.

d. Invasion of bone (as distinct from pressure atrophy and necrosis) may result in subperiosteal and intramedullary extension of the sarcoma superiorly and inferiorly; therefore, amputation through or above the joint with which the affected bone articulates is indicated.

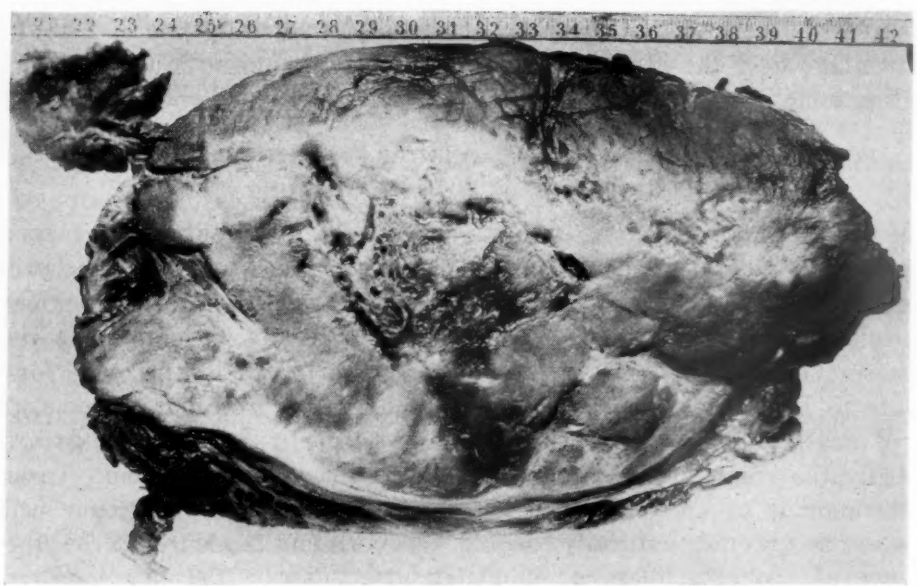
If the sarcoma involves the elbow, or necessitates removal of the elbow, leaving only a stump of the upper arm, the conventional midhumeral amputation or shoulder-joint disarticulation should be abandoned, usually, in favor of the safer, more radical, and only equally crippling interscapulothoracic amputation. The arguments for this conclusion are: the size of axillary lymph nodes, the tendency of certain sarcomas to extend centrifugally upward along the fascial and intermuscular planes, and, finally, the small advantages in possessing the stump of the upper arm and shoulder other than the cosmetic one of serving as a coat hanger. An artificial limb of this type cannot be appended with good function other than to hook and carry. We would delete the operation of humeral disarticulation from the category of cancer surgery; there is no circumstance in which interscapulothoracic amputation for malignant tumors of the upper extremity is not a better operation.

In the case of the lower extremity, the various features of the sarcoma and its treatment should be weighed with care. More importance is given to the conservation of the upper thigh than to that of the upper arm, because even a small stump will permit the comfortable wearing of an artificial limb. The ability to walk with a prosthetic extremity gives this type of amputation an advantage over the hip joint disarticulation, although even after this latter operation some proud patients will persist in wearing a cumbersome artificial leg.

PULMONARY LOBECTOMY AND SEGMENTAL EXCISION FOR METASTATIC RHABDOMYOSARCOMAS OF THE LUNG

Many patients with sarcomas of the soft parts die of pulmonary metastases rather than of complications attendant on the continued growth of the primary tumor. Indeed, 3, 4, or 5 years may elapse after successful local treatment of the original rhabdomyosarcoma by dissection or amputation before the visceral metastases become manifest. It has not been an unusual experience for such patients to have no evidence of locally recurrent or residual sarcoma at the time of death. Spherical metastases in the parenchyma of the lungs are undoubtedly the result of dissemination through the vascular system. Inasmuch as this manner of spread is probably an embolic shower of tumor cells or particles, one would naturally expect the common sequence to be the appearance of multiple bilateral pulmonary metastases. Perhaps hundreds of tumor emboli may die for every one that survives, and, after a variable latent period, grows in the medium of the lung. In practical experience, however,

A. *B.*



C.

Fig. 20.—*A*, Clinical photograph of rhabdomyosarcoma of the thigh. *B*, Postoperative photograph. The entire muscle group dissected and excised with the sarcoma. *C*, Gross specimen of rhabdomyosarcoma of the thigh.

some patients reveal only 1 or 2 spherical opacities in a single pulmonary lobe and these lesions, often asymptomatic, may have been discovered early through the routine checkup roentgenograms of the chest.

If a sarcoma of the soft parts metastasizes to the lungs as a spherical growth and a single metastatic focus is seen, it is entirely feasible and proper to remove this tumor either by segmental resection or by lobectomy. This procedure would have been condemned a few short years ago, but we practice it today with the knowledge, born of experience, that it has definite palliative value. This treatment is contraindicated in the presence of multiple growths involving both lungs or in the event that the sarcoma is infiltrative in character and causes fixation of the hilus. It has frequently been claimed that the measure of palliation, that is, the average postoperative length of life, is generally better for the excision of secondary or metastatic sarcomas of the lung than it is for the majority of primary bronchogenic cancers.

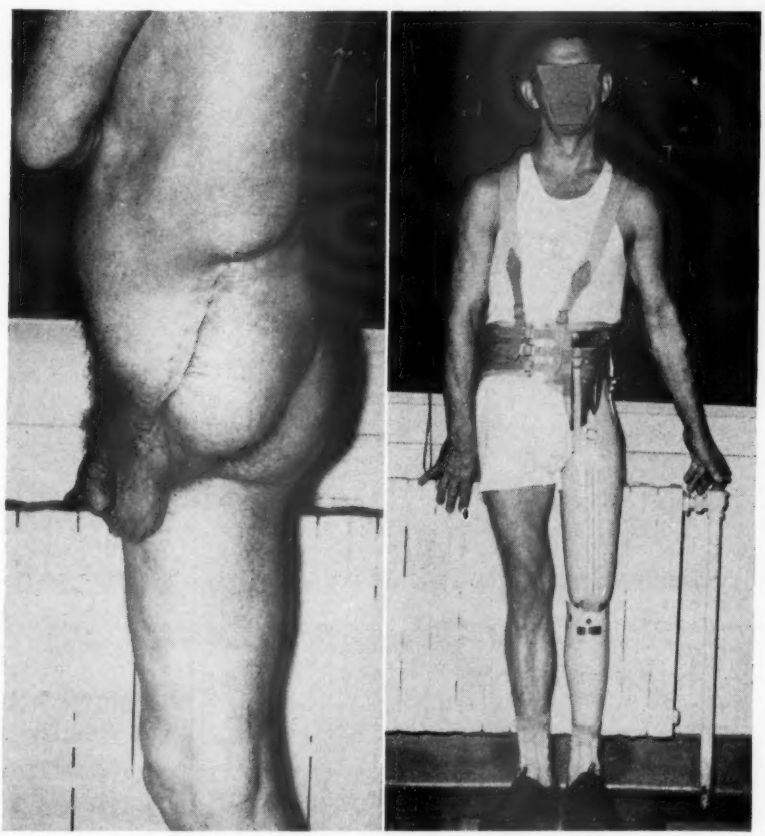


Fig. 21.—Interilioabdominal amputation for rhabdomyosarcoma. Prosthesis for patient after hemipelvectomy.

Before performing a thoracotomy for the removal of such a metastatic tumor, it is a wise precaution to employ tomography (laminagrams) by slicing the lungs radiographically in the anteroposterior and lateral sections because, by doing so, additional cryptic metastatic foci come to light that were not

TABLE VII. RHABDOMYOSARCOMA OF SKELETAL MUSCLES; AGE OF PATIENT IN RELATION TO FIVE-YEAR SURVIVAL WITHOUT DISEASE

AGE	CASES THROUGH 1943			5-YEAR SURVIVALS		DISTRIBUTION OF DETERMINATE CASES						
	ALL CASES	INDETERMINATE CASES	DETERMINATE CASES	NUMBER	PER CENT (BASED ON DETERMINATE CASES)	PRIMARY OPERABLE		RECURRENT OPERABLE		PROPHYLACTIC IRRADIATION		INOPERABLE
						NUMBER	5-YEAR CURES	NUMBER	5-YEAR CURES	NUMBER	5-YEAR CURES	NUMBER
10 years and less	3	1	2	1	50.0	0	0	0	0	1	1	1
11 to 20 years	2	0	2	2	100.0	0	0	1	1	1	1	0
21 to 30 years	5	0	5	3	60.0	2	1	2	1	1	1	0
31 to 40 years	6	1	5	4	80.0	1	1	3	3	0	0	1
41 to 50 years	18	4	14	2	14.3	2	0	8	2	0	0	4
51 to 60 years	22	2	20	7	35.0	5	1	10	5	2	1	3
61 to 70 years	13	3	10	3	30.0	3	1	5	2	1	0	1
71 years and over	8	1	7	0	0.0	3	0	2	0	0	0	2
Total cases	77	12	65	22	33.8	16	4	31	14	6	4	12

TABLE VIII. RHABDOMYOSARCOMA OF SKELETAL MUSCLES; TYPE OF TREATMENT IN RELATION TO FIVE-YEAR SURVIVAL WITHOUT DISEASE BASED ON DETERMINATE CASES THROUGH 1943

TYPE OF TREATMENT	TOTAL CASES			PRIMARY OPERABLE			RECURRENT OPERABLE			INOPERABLE CASES
	TOTAL CASES	5-YEAR CURES		TOTAL CASES	5-YEAR CURES		TOTAL CASES	5-YEAR CURES		
		NUMBER	PER CENT		NUMBER	PER CENT		NUMBER	PER CENT	NUMBER
Excision only	7	4	57.1	3	2	66.7	4	2	50.0	0
Excision and irradiation	21	7	33.3	8	1	12.5	13	6	46.2	0
Amputation	6	3	50.0	2	0	0.0	4	3	75.0	0
Dissection	6	3	50.0	2	1	50.0	4	2	50.0	0
Interscapulothoracic amputation	5	1	20.0	1	0	0.0	4	1	25.0	0
Hip joint disarticulation	2	0	0.0	0	0	0.0	2	0	0.0	0
Postoperative prophylactic irradiation	6	4	66.7	0	0	0.0	0	0	0.0	0
Irradiation only	10	0	0.0	0	0	0.0	0	0	0.0	10
No treatment given	2	0	0.0	0	0	0.0	0	0	0.0	2
Total cases	65	22	33.8	16	4	25.0	31	14	45.2	12

visible in the conventional anteroposterior and lateral views of the chest. The time and expense of routine laminagraphy under these circumstances may be wise expenditures if it decides the surgeon against futile attempts at palliative resection of pulmonary metastases.

END RESULTS OF TREATMENT

Previous reports and opinions concerning the prognosis of rhabdomyosarcomas have been universally pessimistic. Palumbo, Leibovitz and Corcoran declared there were no known instances of cure of this tumor. Arthur Purdy Stout, in reviewing 121 collected cases, of which 108 underwent treatment, found only 4 patients to survive the 5-year period of definitive cure; of these 4 patients, 1 was treated by amputation, 1 by excision alone, and 2 by excision and radiation therapy. In contrast to these poor results, we have 22 of 65 determinate cases whose treatment was conducted by us after a definite pattern,

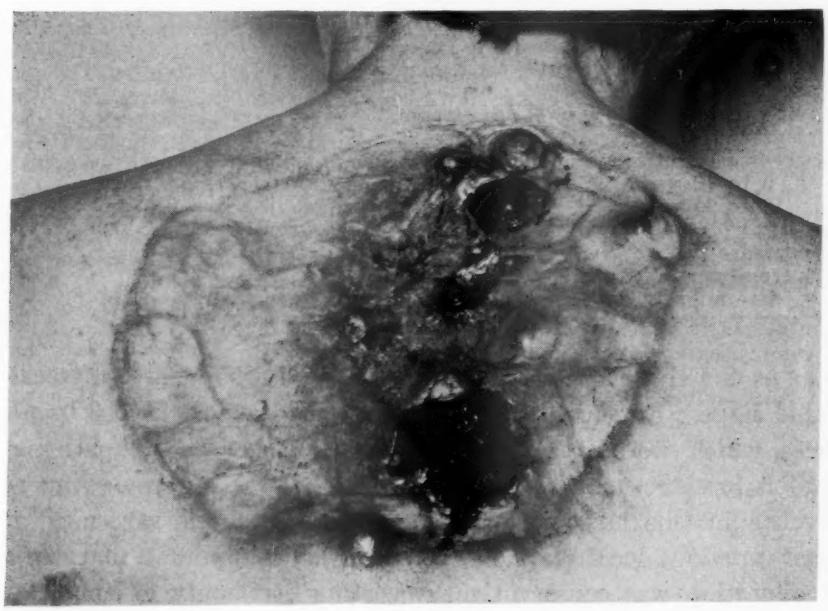


Fig. 22.—Multiple recurrences following wide and deep excision of rhabdomyosarcoma, a characteristic feature in the natural history of the disease.

who are now living and well for more than 5 years from the date of primary treatment without recurrence during the elapsing interval. Five of these 22 patients survived for more than 10 years. This cure rate of 33.8 per cent is the highest yet reported in medical literature. Twelve of these patients had the upper extremity involved, 8 of the rhabdomyosarcomas were situated on the lower extremities, and 2 were on the trunk. The curability of rhabdomyosarcomas in the arm was 3 times as great as the curability for tumors located in the thigh. An explanation of this disparity lies in the early recognition and more prompt acceptance of surgery for tumors of the upper extremity.

Contrary to the generally accepted opinion, the prognosis for rhabdomyosarcomas is better in childhood and early life than it has been in patients of

middle and later life. This paradox has long been known at the Memorial Hospital. No explanation is available for the disparity in survival rates in patients of these different age distributions.

The good end results deserve special attention in view of the distribution of these 65 determinate cases in the groups of primary operable, recurrent operable, and inoperable, stages of the sarcomas at the time of application for treatment. Twelve of these patients had definitely inoperable sarcomas at the time they applied to us: 10 of these patients received irradiation only and 2 received no therapy other than symptomatic relief. Only 16 of the 65 cases were classified as primary operable and 31 patients, or almost half of them,

TABLE IX. RHABDOMYOSARCOMA OF SKELETAL MUSCLES; FIVE-YEAR END RESULTS

Total cases seen through 1948					100
Indeterminate cases through 1948					35
(Patients refusing treatment, not completing treatment, lost track of or treated elsewhere.)					
Determinate cases through 1943, for evaluating five-year cures					65
Failures—died with disease				41	
Living without disease under five years after treatment for recurrence				2	
Successful results—without disease five years or more				22	
5 to 10 years	17	Primary operable cases	4		
10 to 15 years	5	Recurrent operable cases	14		
		Prophylactic x-ray therapy	4		
Five-year cure rate	22/65				
(Successful results divided by determinate cases through 1943)		33.8 per cent			

applied to us for treatment with locally recurrent rhabdomyosarcomas still in an operable stage. Fourteen of these patients had experienced 3 or more local recurrences which were treated by surgical excision and 2 patients in this group had 5 local recurrences treated by dissection. In reviewing the cause of recurrence in this large group of recurrent, operable sarcomas who came to us after previous local excision elsewhere, it is apparent that the previous surgical dissection was conservative, consisting commonly of enucleation with no adherence to the rules for radical surgical dissection as given in detail in another section of this paper. A review of Table VIII would indicate that if recurrence develops following a local conservative procedure, the patient does not necessarily lose his life because our records show that 14 of these 31 patients, or 45.2 per cent, with recurrent operable rhabdomyosarcoma are living and well 5 years after they applied to us for treatment. This 5-year survival rate is higher than was obtained in the group of patients with primary operable rhabdomyosarcomas in which we had the first opportunity for treatment. The paradox of securing higher cure rate for recurrent operable sarcomas than for primary operable sarcomas in our experience is explained by the fact that those patients whom we saw without previous surgical treatment had more advanced tumors in such a location and extent as to discourage surgeons from attempting a simple enucleation.

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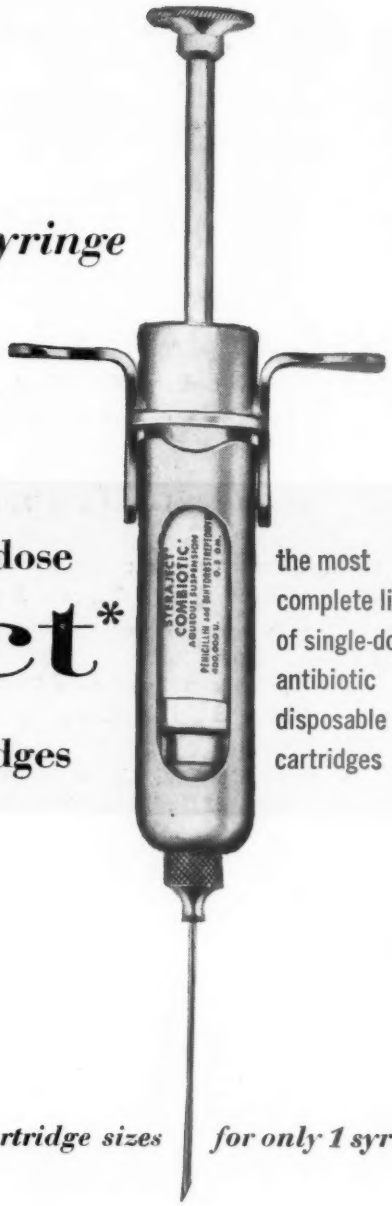

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